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H OWEN THOMAS — MORE THAN AN ORTHOPEDIC SURGEON

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Evaluation of Antibiotic Therapy

CHESTER S. KEEFER*

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A daily problem for all physicians is the selection of the most effective antibiotic for the treatment of infections. In this essay, the author discusses the five antibiotics in common use today and talks about the oral versus the parenteral administration of penicillin. Other topics, such as synergism and antagonism, combined therapy and prophylactic treatment, are covered.

All physicians are confronted daily with the problem of the selection of an antibiotic for a specific patient. To use these agents with the greatest efficiency and with the lowest cost to the patient, it is essential that a proper etiologic diagnosis be made and the best drugs be selected and used. This is not always an easy problem, but it is well to know the relative merits of each antibiotic.

There are five antibiotic drugs in common use today—penicillin, streptomycin, aureomycin, CHLOROMYCETIN and terramycin. Each one has a definite place in therapeutics. I shall begin the discussion with a few words about the common modes of administration.

METHODS OF ADMINISTRATION

Penicillin, aureomycin, chloromycetin and terramycin are given by mouth for the treatment of systemic infections. All of them are absorbed from the gastrointestinal tract. Streptomycin is also given by mouth for its local effect in reducing the bacterial population of the intestine; it is not absorbed.

Penicillin and streptomycin are injected intramuscularly for the treatment of systemic infections, and aureomycin and terramycin can be injected intravenously when the material is properly prepared.

In selecting any of these agents, it is well to remember that penicillin is the only antibiotic that is still being dispensed and prescribed in units rather than by weight. This is unfortunate but understandable because the standards of assay were developed with the use of impure and relatively crude penicillin and before the pure crystalline product had been isolated. It is known now that 1 gm. of crystalline penicillin G is equivalent to 1.5 million units. Therefore, when 300,000 units are prescribed once daily only 0.2 gm. or 200 mg. are being given. Penicillin is highly effective when given by mouth, and I shall discuss oral administration because it is a convenient way to administer this highly potent drug.

To understand why penicillin has not been used more widely for oral medication it is necessary to know something about the background and development of penicillin therapy. At the

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beginning there was very little penicillin available for clinical trial. It was an impure but nontoxic product and relatively unstable when compared to the crystalline penicillin. Moreover, preliminary studies showed that some of the penicillin ingested by mouth was inactivated by the acid gastric juice. It was demonstrated, however, that penicillin was absorbed from the gastrointestinal tract and in patients with achlorhydria the amount absorbed was greater than when the contents of the gastric juice were acid. McDermott et al.[1-2] found, however, that only a small amount of penicillin ingested by mouth was inactivated by the gastric juice. Some was destroyed in the gastrointestinal tract and some passed with the stools. In spite of these facts it was shown that 20 to 30 per cent of the penicillin was absorbed and that the plasma concentration was the same following oral administration as it was following intramuscular injection when three to five times as much penicillin was given. During a period of scarcity of penicillin its oral administration was uneconomical and wasteful. This period has passed long since.

It should be pointed out that comparable plasma concentrations of penicillin do not necessarily mean therapeutic concentrations, nor therapeutic requirements. The most important guide to therapy is the clinical response of the patient. Experience has established certain oral dosage schedules and the amount of penicillin that is needed for many infections. Aside from therapeutic efficiency it should be stressed that penicillin by mouth causes few or no disagreeable side reactions and the incidence of hypersensitivity is less than when it is exhibited intramuscularly.

Oral penicillin is effective in the following diseases.

Gonorrhea—100,000 units (.066 gm.—66 mg.) twice a day

Hemolytic streptococcic infections:

Erysipelas—200,000 units three times a day (.133 gm.—133 mg.)

Scarlet fever—200,000 units three times a day

Tonsillitis—200,000 units three times a day

Otitis media—200,000 units three times a day

Staphylococcic infections—400,000 units three times a day

Pneumococcic infections—200,000 to 400,000 units three times a day

Vincent's angina—200,000 units three times a day

It is plain, then, that penicillin can be given to patients by mouth for the treatment of mild and moderately severe infections and much less is required by weight to produce positive effects than when any of the other antibiotics are used.

SELECTION OF ANTIBIOTICS

I would weary you if I were to review and discuss each antibiotic in any detail, but I want to arrest your attention and fix it on some of the general problems of selection.

First, penicillin continues to be the antibiotic of choice for the treatment of all gram-positive infections due to staphylococci, hemolytic streptococci, pneumococci, subacute bacterial endocarditis due to nonhemolytic streptococci, as well as the drug of choice for the treatment of all cases of gonorrhea and syphilis. The present trends are to use either the oral dosage forms or the procaine salt of crystalline penicillin G in aqueous suspension. That is my first point. There is less sodium and potassium penicillin G in aqueous solution being used for parenteral therapy. That is my second point. And my third and final point is that the tendency is to increase the total amount of penicillin given with each injection or by mouth and to lengthen the interval of time between doses.

Streptomycin continues to be the most potent agent against tuberculosis. No drug and no other antibiotic approaches it in potency. Its action may be assisted by PAS, TB_1 or the sulfones, but none is superior.

Chloromycetin is the best anti-infective drug for the treatment of typhoid fever. None of the other antibiotics are nearly so effective and all cases of typhoid fever should be treated with this agent. Recent studies by Woodward and his associates[3] are highly suggestive that this effect can be accelerated by simultaneous administration of cortisone.

I want to turn your attention now to a comparison of aureomycin, chloromycetin and terramycin. In the first place, it can be said that aureomycin and terramycin are more potent against gram-positive organisms than against gram-negative ones. Chloromycetin is more active against gram-negative infections than against gram-positive infections. All three antibiotics have a positive action against both gram-positive and gram-negative micro-organisms.

All three of these antibiotics are equally active in the treatment of the rickettsial diseases, primary atypical pneumonia, lymphogranuloma

TABLE 1

COMBINED THERAPY

Penicillin and sulfonamides	Bacterial meningitis Pneumococcus Streptococcus Staphylococcus Actinomycosis Mixed wound infections
Penicillin and streptomycin and sulfonamides	Peritonitis and mixed bacterial wound infections Subacute bacterial endocarditis (Enterococcus)
Streptomycin and sulfonamides	Mixed bacterial wound infections Brucellosis
Streptomycin and aureomycin	Brucellosis
Streptomycin and para-aminosalicylic acid	Tuberculosis
Streptomycin and PROMIN	Tuberculosis
Penicillin and aureomycin Penicillin and chloramphenicol Penicillin and terramycin	Probably should not be used in combination until more information is available

venereum group of viruses, as well as in granuloma venereum and mixed urinary tract infections. In my opinion there is no choice between the three.

All three of these antibiotics are useful in the treatment of undulant fever, and there is very little choice between them. There is some evidence that combining any one of these agents with dihydrostreptomycin produces better results than using any one of them alone. That is to say, there are fewer relapses.

Aureomycin or terramycin has been useful in the treatment of staphylococcic infections that are resistant to penicillin.

In the treatment of lobar pneumonia, penicillin, aureomycin and terramycin have been equally effective, and there has been little difference in the results when comparable cases have been studied.

In the management of hemolytic streptococcal infections penicillin is superior to all other antibiotics although positive results have been obtained with aureomycin, chloromycetin and terramycin.

Tularemia responds most promptly to streptomycin and in my opinion this drug should be used in all cases. Aureomycin, terramycin, and chloromycetin are also active. Therefore, we have four good anti-infective agents against this disease.

Streptomycin and chloromycetin are the two most potent antibiotics for the treatment of influenza bacillus infections. Chloromycetin by mouth has been used successfully in the treatment of influenza bacillus meningitis. When streptomycin is used in the treatment of influenza meningitis it should be given both intramuscularly and intrathecally. Also it is well to combine it with sulfadiazine. The infection also responds to aureomycin. Terramycin is not recommended.

Streptomycin and aureomycin are the two drugs to be used in cases of Friedlander bacillus infections.

Urinary tract infections are complicated infections, usually due to gram-negative organisms. The common ones are the *Colon bacillus, Aerobacter aerogenes, Bacillus proteus* and *Bacillus pyocyaneus*. Streptomycin has the most striking benefit in all of these infections and maximum results are obtained within five to seven days in patients without obstructive lesions of the genitourinary tract. Only a very few strains of *B. proteus* and *B. pyocyaneus* are sensitive to aureomycin, chloromycetin or terramycin. Many of the other urinary tract infections will respond to any one of the three agents mentioned, but none is superior to streptomycin. They have the advantage, however, that they can be given by mouth.

Amebiasis has been controlled with aureomycin, terramycin and bacitracin.

SYNERGISM AND ANTAGONISM

It is common practice for physicians to use combinations of antibiotics, or combinations of antibiotics and the sulfonamides. This is done with the hope that two agents will be more effective than one, and if the effect is not synergistic it is hoped that it will be at least additive. A number of combinations have been studied in the test tube as well as in man and many more studies are needed before we can make any precise statements concerning superior results of combined antibiotic therapy. However, there is suggestive evidence that penicillin and streptomycin[4] are more potent when used in combination for the treatment of subacute bacterial endocarditis than when penicillin is used alone. This is especially true in cases of subacute bacterial endocarditis due to the enterococcus. Also

Herrell and his colleagues[5] have reported that aureomycin by mouth and dihydrostreptomycin intramuscularly are more effective in the treatment of brucellosis than aureomycin alone. We have had one patient with enterococcic endocarditis who was resistant to penicillin treatment alone but who responded to both penicillin and terramycin when given together.

Test tube experiments have shown further that some strains of streptococci that are resistant or are not killed by penicillin may actually grow at a greater rate or show slower killing when aureomycin or chloromycetin is added to the medium.

The interpretation of such experiments is difficult, but Hunter[4] suggests that the explanation may be that penicillin has been shown to kill only those organisms which are in the process of active multiplication. When another agent is present—like aureomycin or chloromycetin—that renders them static (inhibits but fails to kill), then organisms are no longer killed by penicillin.

In infections where the final death of the organisms is important such as in subacute bacterial endocarditis, the combination of two drugs like streptomycin and penicillin that cause complete killing of organisms may be important. In cases where inhibition of growth of organisms is adequate for recovery, then this is most often accomplished by using one antibiotic rather than two. At least that is the implication.

Penicillin and sulfadiazine have been used most extensively in the treatment of bacterial meningitis. The evidence is suggestive but not conclusive that combined therapy is better than penicillin alone. In the interpretation of results one must naturally take into account the total dosage of each agent used and whether or not intrathecal therapy has been used at the same time, because Dowling et al.[6] have shown that massive doses of penicillin given intramuscularly without intrathecal injections or without sulfonamides are also adequate in cases of pneumococcal meningitis. The same combined treatment is said to be needed for actinomycosis.

Streptomycin and sulfonamides have been used in combination most often in the treatment of influenza bacillus meningitis and in brucellosis. However, it would appear that chloramphenicol alone is adequate in *Hemophilus influenzae* meningitis and that aureomycin and dihydrostreptomycin are more effective in brucellosis than streptomycin and sulfadiazine.

USE OF ANTIBIOTICS IN PROPHYLAXIS

Antibiotics are used very widely for the prophylaxis of infections. Certain criteria have been developed for their use in surgical patients in our clinic at the Massachusetts Memorial Hospitals and they are as follows:

First, all patients who have had an operation of long duration, i.e., two hours or longer, receive 300,000 units of procaine penicillin G daily for five days. Also any patient who has had an acute respiratory infection within two weeks prior to operation receives 300,000 units of penicillin the day before operation, and this dosage level is maintained for five days after operation. Furthermore, all patients who have upper abdominal operations, or who have operations in which the pleural cavity is entered, receive prophylactic penicillin for five days after operation. All patients who have wound contamination at time of operation receive local treatment of the contaminated area with a solution of 5 per cent SULFAMYLON and 200 mg. streptomycin per cubic centimeter, followed by parenteral treatment with 1.5 gm. penicillin and 1 gm. streptomycin daily for five days.

When resection of the large intestine is contemplated, SULFASUXIDINE or SULFATHALIDINE is given daily for four days prior to operation and continued for five days after operation. This is less expensive to the patient than oral antibiotics such as aureomycin, terramycin or polymyxin, and in our experience just as effective.

In patients who are subjected to pneumonectomy or lobectomy penicillin prophylaxis is carried out for several days prior to operation and continued for seven days after operation.

Prophylactic antibiotic therapy in medical diseases is most important in the prevention of gonorrhea, streptococcic infections and recurrences of rheumatic fever, and in the reduction of bacteremia following tooth extraction. It is important to reduce the incidence of bacteremia in patients with organic valvular heart disease who may develop bacterial endocarditis following tooth extractions.

It has been demonstrated that 250,000 units of penicillin by mouth will prevent gonorrhea if it is taken within 6 to 12 hours of exposure.

Either aureomycin or penicillin is a good prophylactic agent for the reduction of bac-

teremia following tooth extractions. The recommended dose of aureomycin[7] is 2 gm. a day for three days in divided doses. The last dose before the operation should be given not earlier than three hours before surgical intervention.

A most careful study of the effect of penicillin on the bacteremia following dental extraction has been made by Glaser, Dankner, Mathes and Harford.[8] It is their proposal that all patients with rheumatic or congenital heart disease, who are to have dental extraction, should receive large doses of penicillin prior to operation and their patients received 50,000 units of penicillin intramuscularly every two hours day and night for 24 hours before extraction—total dose of 600,000 units. The last dose was given approximately 20 minutes prior to extraction.

In summary then, it is well in the selection of antibiotics to choose the agent that is likely to be the most effective in the shortest period of time. Also, it should be recalled that penicillin is extremely effective when given by mouth for the treatment of mild and moderately severe infections due to gram-positive micro-organisms—200,000 to 400,000 units three times a day is usually adequate.

The use of various combinations of antibiotics needs to be explored further before any definite statements can be made concerning the optimum dosage and the most effective combinations.

Also, careful studies in prevention should be carried out in medical and surgical infections.

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PIONEER ORTHOPEDIC SURGEON ALSO NOTED FOR ADVANCES IN MEDICAL TREATMENT

In writing of Hugh Owen Thomas, Sir Arthur Keith said: "Yet the great legacy Thomas has left to medicine would be not his splints or appliances, his principles, his practical application of anatomy or of physiology, but his personal care in the service of his patients, his peculiar ability as a biological surgeon, his remarkable gift for taking pains."

Dr. Thomas is, however, best known for his many contributions to modern orthopedic surgery, a field which he influenced with the appliances he developed and the fundamental precepts he pronounced and taught.

Though always a controversial figure, he is remembered, as Sir Robert Jones said in the first Hugh Owen Thomas Memorial Lecture, as "an inspiration to all who fight for new principles; for, with scarcely a helping hand, he struggled through the stormy waters which face all pioneers and died having added luster to the profession he loved."

Reprints of Edmund Kopietz' cover painting, suitable for framing, may be obtained from *Postgraduate Medicine,* 516 Essex Building, Minneapolis 3, Minnesota. $1.00.

The "Performance Index"

AS A METHOD FOR ESTIMATING EFFECTIVENESS OF REDUCING REGIMENS

NORMAN JOLLIFFE[1] AND ELMER ALPERT[2]

DEPARTMENT OF HEALTH, NEW YORK CITY

It is generally accepted that the essential component of every reducing regimen is a calorie deficit.[1] By metabolic studies the loss of adipose tissue over a period of time, in an obese person maintained on a sub-calorie diet, otherwise adequate, has been shown to be directly proportional to the calorie deficit. This loss of adipose tissue can be predicted with remarkable accuracy. These metabolic calculations are based on the fact that 1 gm. of adipose tissue yields an average of 7.7 calories,* one pound of adipose tissue yields 3500 calories and 1 kg. yields 7700 calories. Therefore, a deficit of about 3500 calories leads to the metabolism of a pound of adipose tissue, and a deficit of about 7700 calories leads to the metabolism of 1 kg. of adipose tissue. This is true whether the calorie deficit is acquired over one day, one week, one month or, for that matter, one year. It is therefore possible, when the calorie deficit is known, to predict with remarkable accuracy the loss of adipose tissue over a period of time.[2-4]

All methods of reducing the obese of excess fat are effective only insofar as they aid in producing and maintaining a calorie deficit. A calorie deficit can be obtained either by increasing the calorie expenditure or by decreasing the calorie intake, or by both methods. There is an exaggerated idea of the value of exercise in producing a calorie deficit. For the average person a walk of one mile at the rate of 2 miles per hour leads to the expenditure of 100 extra calories. Therefore, to lose 2 pounds of adipose tissue by this type of exercise alone, the average person would have to walk 10 extra miles each day for one week without increasing the food intake. This is difficult because exercise usually increases the appetite. Therefore a considerable and sustained increase in calorie expenditure by exercise for most obese persons is impractical. On the other hand, to lose 2 pounds of adipose tissue by diet while maintaining the same calorie expenditure—that is, without additional exercise—the obese person needs to eat daily for one week 1000 calories less than the calorie expenditure. For most obese persons this is easier than the equivalent amount of exercise and does not require daily 5 extra hours of walking. Therefore, most reducing regimens simply are based on the production of a calorie deficit by a reduction of calorie intake below calorie expenditure without simultaneously increasing the calorie expenditure.

Adjuvants to the sub-calorie diet, whether medicinal, physical, psychologic or educational, are valuable only insofar as they increase the calorie expenditure or aid the patient in control of appetite so as to adhere to the prescribed diet. Measurements of the effectiveness of these adjuvants to the sub-calorie diet have been noteworthy for their unreliability. Therefore a method for the quantitative comparison of the effectiveness of various reducing regimens in groups of obese people is needed.

To illustrate some of the problems that arise in comparing the relative effectiveness of weight-reducing regimens, let us consider the follow-

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[2]Physician, Nutrition Clinic, Bureau of Nutrition, New York City Department of Health.

*One gram of pure fat in metabolism yields 9.3 calories. Adipose tissue, however, contains a variable amount of water averaging about 17 per cent, so that the calorie value of 1 gm. of adipose tissue averages 7.7 calories.

ing hypothetical study. Three groups of obese people all have prescribed for them an identical diet averaging 1000 calories daily but are given three different anorexic agents. Over a period of eight weeks, these three groups of persons lose an average of 1.5, 1.75 and 2.0 pounds each per week. This average weekly loss of weight does not necessarily indicate the relative effectiveness of the three anorexic agents. If the calorie expenditure of the three groups of subjects is approximately equal, then the greater loss of weight in the third group would indicate a closer adherence to the prescribed 1000-calorie diet. On the other hand, had the average daily calorie expenditure of the third group been 200 calories greater than the second group, and 400 calories greater than the first group, a not unusual situation, then it may be calculated by methods described later that the 2.0 pounds per week average loss of weight represents a worse performance for group three than 1.75 pounds per week for group two, and 1.5 pounds for group one. If the deviation in calorie expenditure was of this magnitude in the three groups, then the loss of 1.5 pounds per week in the first group represented a better performance, that is adherence to the prescribed 1000-calorie diet, than either group two or group three. This example illustrates the fallacy of attempting group comparison on the basis of crude rate of weight loss without consideration of group similarity in energy expenditure.

Since the calorie expenditure is the result of at least six variables—age, sex, height, weight, basal metabolism and physical activity—it is, for practical purposes, almost impossible to obtain groups of patients matched in all these variables. On the other hand, unless the groups of subjects are so matched, comparative results based upon the average loss of weight per week lack significance.

SINCE the variables constituting the total calorie expenditure can be estimated with a reasonable degree of accuracy, it follows that an estimate of the total calorie expenditure also can be made within the limits of reasonable accuracy. By deducting the calorie intake from the calorie expenditure, the calorie deficit can be calculated. From the calorie deficit the predicted weight loss can be estimated for each subject. Then, following reduction, a comparison of the observed weight loss with the predicted weight can be made and converted into an index representing the effectiveness of management. Such an index we propose to label the "performance index." Perfection by the "performance index" is the predicted rate of adipose tissue loss per week had both the food intake and the total calorie expenditure been known.

NORMAN JOLLIFFE

The performance index assumes that total weight loss and the total adipose tissue loss are for practical purposes either identical or parallel. In some persons they are neither identical nor parallel and these subjects should be excluded. The subjects to be excluded are persons with more than minimal edema where loss of adipose tissue may result in loss of edema fluid or where loss of edema fluid would not represent loss of adipose tissue. Therefore patients with significant amounts of edema cannot be used for comparative studies unless water balance measurements are included, which for ambulatory patients are not practical. Also to be excluded are persons with a negative nitrogen balance. A negative balance of 1 gm. of nitrogen may be accompanied by the loss of as much as 50 gm. of water. Therefore patients with a negative nitrogen balance, whether due to disease or to inadequate dietary protein, cannot be used in these studies unless nitrogen and water bal-

ELMER ALPERT

ance determinations are simultaneously carried out, which are impractical for ambulatory patients. The negative nitrogen balance that frequently occurs during the first few days of a reducing diet, even though the diet is high in biologically good protein, can be overlooked for practical purposes if the minimum period of observation is of sufficient length to minimize its relative effect. A four-week period is generally sufficient for this purpose. A third factor to be considered is a temporary shift in water balance which sometimes occurs in obese patients losing adipose tissue.[1] These shifts, although annoying and sometimes discouraging to both patient and physician, are seldom over a few days' duration, and as a rule spontaneously correct themselves. By making the period of observation at least four weeks, these shifts in water balance are largely negated and total weight loss, for practical purposes, can be interpreted and recorded as adipose tissue loss.

THE GROUP PERFORMANCE INDEX

The method developed by Wilder[2] of predicting the rate of weight loss in any individual subject on a sub-calorie diet, otherwise adequate, can be applied with slight modifications to groups of obese subjects which do not include edematous persons or those in negative nitrogen balance. To make Wilder's method more easily applied to group studies, certain minor modifications have been made by us. The first of these modifications is that all calculations are made for a 25-pound decrement of weight loss instead of the 30 to 50-pound decrements used by Wilder. The figure of 25 pounds is taken because that loss of weight reduces the energy requirement by about 100 calories daily. Larger amounts are not unimportant while smaller amounts do not introduce a significant error in the predicted weight loss.

The basal energy requirement is calculated from the actual weight at the beginning instead of at the end of each period. The time required to lose 25 pounds is then determined and plotted on graph paper. When the patient is less than 25 pounds overweight the amount of weight to be lost is determined and similarly plotted.

Correction is also made for significant deviations in basal metabolic rate. If the deviation is greater than plus or minus 15 per cent, addition or subtraction of the observed percentage change is applied to the basal energy requirement. These corrections for abnormal basal metabolic rates are made because when present they are large enough to be important. No corrections are made in the basal energy requirement if the basal metabolic rate has not been determined or if the rate is between +15 and −15, for to neglect them does not introduce significant errors in the predicted weight loss.

The method of determining the performance index for group comparisons can be summarized as follows:

1. For each individual determine the basal energy requirement by the Boothby and Berkson Food Nomogram[5] (Figure 1). The initial weight at the beginning of each 25-pound decrement in weight is used for the calculation. To the basal calorie requirement a percentage correction is added or subtracted if the basal metabolic rate is above +15 per cent or below −15 per cent. No correction is made if the basal metabolic rate is between these figures or if it is unknown. To the corrected basal calorie requirement is added 20 to 70 per cent (usually 40 or 50 per cent) according to Table 1 to cover the calories required for activity. The resulting figure represents the estimated daily calorie expenditure.

FOOD NOMOGRAM

Directions: The standards for age are arranged on the basis of the common method of expressing age as of the last birthday. To determine the desired calorie allowance, proceed as follows: (1) Locate the weight on Scale I by means of a pin stuck through the eraser of a lead pencil. (2) Place the edge of the ruler against the pin and swing the other end of ruler to the patient's height on Scale II. (3) Transfer the pin to the point where the ruler crosses Scale III which gives the surface area in square meters (this value need not be read). (4) Holding the ruler against pin on the surface area scale, swing the left hand end of the ruler to the patient's standard for age and sex given on Scale IV. (5) Transfer the pin to where the ruler now crosses Scale V which gives the basal heat production of the patient for 24 hours and represents the calories of food required by the fasting patient when resting in bed (basal calories).

The calories necessary for activity bear a percentage relationship to those demanded for the resting condition. The so-called "white collar worker" when at work will need about 50 per cent more than his basal calories. When activity is restricted, as in the hospital, the extra calories necessary will range from 10 to 30 per cent of the basal calories. Therefore (6) estimate the per cent of calories above the basal and locate this point on Scale VI. With the ruler connect this point with the point located previously on Scale V, and where the ruler now crosses Scale VII read the amount of food calories to be provided by the diet.

W. M. Boothby and J. Berkson, October, 1933.

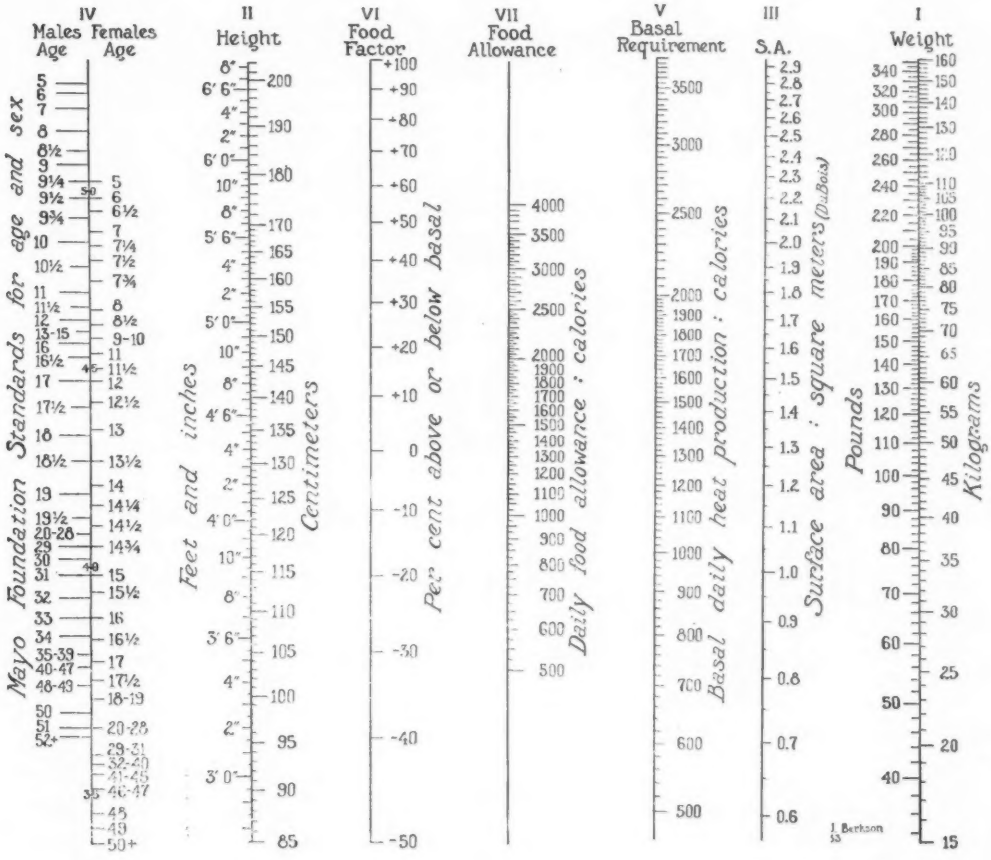

FIGURE 1. The Boothby and Berkson Food Nomogram. (Reproduced by courtesy of Dr. Joseph Berkson. Copies of this food nomogram may be obtained from the Division of Biometry and Medical Statistics, Mayo Clinic, Rochester, Minnesota.)

TABLE 1

ALLOWANCE FOR ACTIVITY

Per Cent Increase to be Added to Basal Calories at Present Weight to Obtain Predicted Energy Expenditures

20	*per cent* for people at house or "bed rest." This figure is used when the person is confined to bed, or room or to a wheel chair such as might occur following a fracture of the leg, a crippling type of arthritis, hemiplegia, heart disease and in early convalescence from an illness.
30	*per cent* for people at moderately restricted activity but who are up and about. This generally includes people in late convalescence who are not confined to the house but who are permitted to sit on the lawn, take short motor trips, take short walks or to be a sports spectator. This group also includes most retired elderly people who voluntarily, or on doctors' orders, restrict physical activity to the minimum sufficient to prevent boredom.
40	*per cent* for people with slightly restricted activity. The largest group here are housewives who do not do their own housework or engage in outside work.
50	*per cent* for people in the following light or home occupations: the white collar occupations, machinery operators, housewives who do their own work, domestic servants, chauffeurs, and similar occupations.
60	*per cent* for people who are moderately heavy workers such as manual laborers, farmers, truck drivers and expressmen. This also applies to most adolescent children who are obese.
70 *to* 100	*per cent* for people who are engaged in heavy work such as stevedores, lumberjacks, steel workers and similar occupations.

2. The difference between the estimated daily calorie expenditure and the prescribed calorie intake derived from a sub-calorie diet otherwise adequate is the "calorie deficit." This figure multiplied by the factor 0.002* will give the predicted loss of weight per week in pounds when calculated on a minimum of four weeks' time and a maximum loss of weight of 25 pounds.

3. Calculate the time in weeks required to lose 25 pounds. When this time is reached and if further loss of weight is indicated, the basal energy requirement is recalculated at that weight for the next decrement of 25 pounds. If the desired loss of weight is less than 25 pounds, then the time required to lose that lesser amount is calculated instead.

4. For each individual determine the performance index by the formula:

$$\frac{\text{observed weight loss}}{\text{predicted weight loss}} \times 100$$

5. The average of the individual performance indexes will give the group performance index. A perfect performance index is 100 and represents the figure that theoretically would be obtained if the calorie expenditure had been accurately predicted and the food intake accurately weighed.

Calculation of the performance index will permit individuals of different sexes, ages, occupations, activities, ideal weights and degrees of overweight to be compared. In normal people any significant deviation from 100, either up or down, represents either an error in the estimation of the calorie expenditure, deviations conscious or unconscious from the diet or temporary shifts in water balance or in intestinal contents.

*The factor 0.002 is derived as follows: One pound of adipose tissue in metabolism yields an average of 3500 calories. The daily calorie deficit multiplied by 7 gives the weekly calorie deficit, which divided by 3500 gives the predicted loss of adipose tissue in pounds for one week, and the equation is: predicted loss of weight per week = daily calorie deficit x 7/3500. The factor 0.002 is the constant derived from 7/3500 and is substituted for this part of the equation. If the weight loss is to be calculated in kilograms per week the equation becomes: predicted loss of weight per week = daily calorie deficit x 7/7700, and the constant factor becomes 0.0009.

ACCURACY OF PREDICTED WEIGHT LOSS WHEN FOOD IS WEIGHED

By applying metabolic calculations to data of patients studied in a metabolism ward, the weight loss of an individual subject can be predicted over a four-week period within an accuracy of 5 to 10 per cent or even less. This fact has been repeatedly demonstrated by Newburgh[1] and his collaborators. That the weight loss can be predicted within clinical accuracy by this method outside the hospital metabolism ward when the food intake is weighed and activity is at a minimum is demonstrated by the following subject:

CASE REPORT

Mrs. C. D., 57 years of age, 5 feet, 3 inches tall, of medium frame; weight 226 pounds; basal metabolic rate +7. The patient had been confined to a bed and wheel chair for seven years because of severe crippling arthritis; during this time she had gained about 100 pounds. General medical examination disclosed no significant defect other than the arthritis. There was no fever, leukocytosis, increased erythrocyte sedimentation rate or anemia. As the patient was confined to her home under the constant care of nurses, she was placed

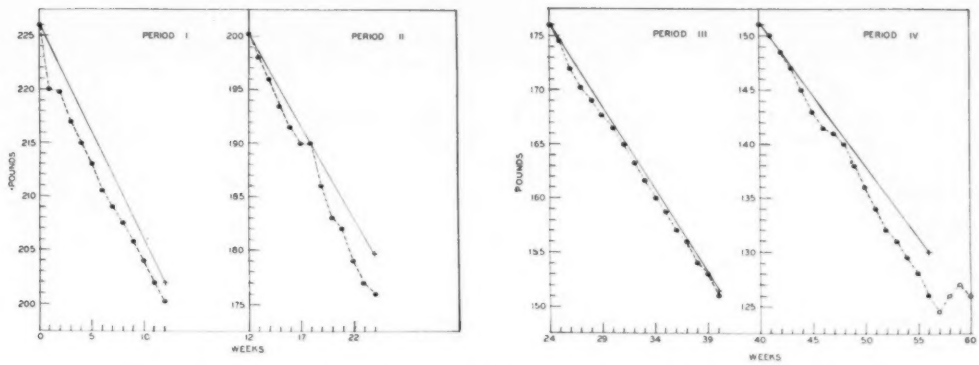

FIGURE 2. Observed (broken line) and predicted weight loss (solid line) for Mrs. C. D.

on a weighed high protein, low fat diet averaging 1000 calories daily, supplemented by one multiple vitamin capsule containing supplementary levels of the essential vitamins. Analgesic drugs were permitted and daily massage was given by the nurse.

The patient was weighed weekly at the same time of day for the next 14 months. The results are presented in Table 2 and Figure 2. During the entire 56 weeks the patient lost 100 pounds; the predicted loss of weight was 91.6 pounds, giving a performance index of 109.6. In the first, second and fourth periods the performance index was 107.3, 111 and 119.3 respectively; in the third period the performance index was 100.8. During this third period a different nurse weighed the diet. It is possible that this person was slightly more generous in the food weighing than the nurse in the other three periods. We feel that this subject demonstrates the practicability of using metabolic calculations for predicting weight loss outside the metabolism ward when the diet is weighed and activity is at a minimum.

ACCURACY OF PREDICTED WEIGHT LOSS IN AMBULATORY SUBJECTS

Very few obese patients can be studied in a metabolism ward, eat from a diet kitchen or have a trained dietitian or nurse weigh the diet. Neither is it practical for the majority of them to be under constant supervision to prevent conscious dietary deviations. Under practical conditions most obese patients have prescribed for them diets which they estimate in terms of household measurements and they are supervised chiefly by their own conscience or by nagging and cajoling relatives and friends. Is it possible under these conditions to predict the loss of weight within practical clinical accuracy? To test this possibility we selected 11 intelligent adult patients, all long-time friends or relatives who had strong motivation for reducing and who we felt could be trusted not to deviate consciously from the prescribed diet. The importance of this fact was stressed and each person took this obligation seriously.

On the first visit the sub-calorie high protein diet was outlined to the patient. From the estimated calorie expenditure and the estimated prescribed dietary calories the calorie deficit was calculated and the predicted weight loss per week was determined. A graph showing the predicted weight loss was prepared. Each subject was told that his weight curve should follow very closely or slightly below the predicted curve as demonstrated by patient C. D. Any time the weight curve crossed to the right of the predicted curve the patient was told that dietary deviations accounted for it. These 11 patients returned each week for weighing and discussion of their dietary and other problems.

In this group of 11 subjects there were 4 men and 7 women, ranging in age from 32 to 60 years. The subjects averaged 27.3 pounds overweight, the amount varying between 9 and 65.5 pounds. They averaged 18.8 per cent overweight, varying from 8 to 45 per cent. The basal metabolic rates were all within normal range. No subject had clinical evidence of edema. Other than a multiple vitamin capsule containing supplementary levels of the essential vitamins and laxatives as previously habitually taken, no medication was prescribed. All subjects were told to continue their usual occupation and degree of physical activity but under no conditions or circumstances to deviate from their prescribed diet. Significant data on each

TABLE 2

SUMMARY OF DATA ON MRS. C. D., AGE 57, HEIGHT 5 FT. 3 IN.

	INITIAL WEIGHT IN POUNDS	PREDICTED CALORIE EXPENDITURE*	DIET IN CALORIES	CALORIE DEFICIT	PREDICTED WEIGHT LOSS PER WEEK (POUNDS**)	WEEKS OBSERVED	TOTAL PREDICTED WEIGHT LOSS (POUNDS)	OBSERVED WEIGHT LOSS (POUNDS)	PERFORMANCE INDEX
1st Period	226.0	1990	1000	990	1.98	12	23.76	25.5	107.3
2nd Period	200.5	1920	1000	920	1.84	12	22.08	24.5	111.0
3rd Period	176.0	1775	1000	775	1.55	16	24.80	25.0	100.8
4th Period	151.2	1655	1000	655	1.31	16	20.96	25.0	119.3
TOTAL							91.6	100.0	109.6

*Based on basal calorie expenditure plus 20 per cent for activity.
**Calorie deficit x 0.002.

subject in this group are given in Table 3.

The predicted total loss of weight for this group of 11 subjects was 216.5 pounds. They actually lost a total of 214.25 pounds, giving a performance index of 98.9. The individual performance indexes varied from 85.2 to 118.6 and all but 2 (subjects 2 and 5) were between 85 and 110. The average of the individual performance indexes was 99.9 with a standard error of the mean of 3.4. The weight loss per week varied from 1.72 pounds (subject 6) to 3.57 pounds (subject 1). However, the performance index for these 2 subjects was 92.6 and 106.9 which is not significantly different. This shows that the uncorrected weight loss per week does not truly express the adherence of the patient to the prescribed sub-calorie diet.

The average weight loss per week for the entire group of 11 subjects was 2.42 pounds. A comparison of the crude weight loss per week with the performance index showed no correlation between the degree of overweight, whether expressed in pounds or in percentage, and the performance index. There were too few subjects maintained on a diet higher than 1000 calories to indicate whether or not the performance index was better on 1000 calories than on somewhat higher calorie intakes.

TABLE 3

SUMMARY OF DATA ON SELECTED GROUP OF 11 SUBJECTS

SUBJECT	SEX	AGE	HEIGHT IN INCHES	ACTIVITY PER CENT (TABLE 1)	INITIAL WEIGHT (POUNDS)	IDEAL OR DESIRED WEIGHT (POUNDS)	POUNDS OVERWEIGHT	PER CENT OVERWEIGHT	PREDICTED BASAL CALORIES	PREDICTED TOTAL CALORIE EXPENDITURE	PRESCRIBED DIET IN CALORIES	CALORIE DEFICIT	PREDICTED WEIGHT LOSS PER WEEK (POUNDS)	WEEKS OBSERVED	TOTAL PREDICTED WEIGHT LOSS (POUNDS)	OBSERVED TOTAL WEIGHT LOSS (POUNDS)	OBSERVED WEIGHT LOSS (POUNDS PER WEEK)	PERFORMANCE INDEX
1	M	48	67½	50	192.75	170	22.75	13	1780	2670	1000	1670	3.34	7	23.38	25.00	3.57	106.9
2	F	50	67	50	193.50	150	43.50	29	1620	2430	1250	1180	2.36	10	23.60	28.00	2.80	118.6
3	F	60	64½	50	192.25	155	37.25	24	1570	2355	1250	1105	2.21	11	24.31	25.25	2.29	103.9
4	M	46	69	50	212.00	182	30.00	16	1880	2820	1200	1620	3.24	8	25.92	26.00	3.25	100.3
5	F	50	62½	50	134.00	125	9.00	7	1310	1965	1000	965	1.93	4	7.72	9.00	2.25	116.6
6	F	60	63	40	147.00	131	16.00	12	1380	1930	1000	930	1.86	9	16.74	15.50	1.72	92.6
7	M	32	68¼	50	172.00	154	18.00	12	1800	2700	1200	1500	3.00	7	21.00	18.00	2.57	85.7
8	F	39	65	50	146.00	134	12.00	9	1460	2190	1000	1190	2.38	6	14.28	13.75	2.29	96.3
9	F	39	58½	50	150.00	123	27.00	22	1380	2070	1000	1070	2.14	12	25.68	23.00	1.92	89.6
10	M	42	65¾	40	209.50	144	65.50	45	1840	2580	1500	1080	2.16	11	23.76	20.25	1.84	85.2
11	F	43	59	50	137.50	118	19.50	17	1340	2010	1000	1010	2.02	5	10.10	10.50	2.10	103.9
TOTALS															216.49	214.25		99.96

This study indicates that highly selected patients who do not consciously deviate from their prescribed diet as estimated by household measurements will lose weight as a group over a minimum of four weeks' time at a rate remarkably similar to that predicted by our modifications of Wilder's method.

Since this group of highly selected patients who did not consciously deviate from their prescribed diet gave a performance index of 99.9 with a standard error of 3.4, this method can be used to test the effectiveness of single variations in the management of groups of patients otherwise similar in whom the calorie deficit can be estimated. It therefore follows that significant deviations from a group performance index of 100 represent deviations from the diet. Since management of obesity resolves itself into methods for obtaining adherence by the patient to the prescribed sub-calorie diet, significant deviations from a performance index of 100 represent a degree of failure of that particular method of obtaining complete cooperation of the patient.

EFFECTIVENESS OF CITRUS FRUIT AS AN ANOREXIC AGENT

To demonstrate the practicability of the performance index as a measure of the effectiveness of a reducing regimen, we studied the use of citrus fruit juice as an anorexic agent. In this study 73 unselected and consecutive subjects referred to us for weight reduction were used. Of this group 42 or 58 per cent returned for at least four consecutive weeks, the minimum time necessary for significant observations.

The management of this group of 42 unselected subjects was identical with the group of 11 selected subjects, except that they were instructed to use 4 ounces of either orange juice or grapefruit juice as an anorexic agent in the late morning 30 to 60 minutes before their noon meal, and in the late afternoon 30 to 60 minutes before their evening meal.

Each subject had prescribed for him a low calorie, high protein diet ranging between 1000 and 1400 calories, plus the citrus juice allowance which we counted as 100 calories daily. At the beginning of weight reduction the predicted loss of weight was made into a graph and the patient was told that his weight curve should follow very closely or slightly below the predicted curve. Any time the weight curve crossed to the right of the predicted curve the patient was told dietary deviations were to blame. The patients returned each week for weighing and for discussion of their dietary and other problems. They were followed for periods of 4 to 13 weeks. In this group of 42 subjects there were 8 men and 34 women, varying in age from 17 to 62 years. They averaged 41.3 pounds overweight, the amount ranging from 11 to 131 pounds. They averaged 29 per cent overweight (6.8 to 91 per cent). A multiple vitamin capsule containing supplementary levels of the essential vitamins was prescribed for each patient. Laxatives, as previously habitually taken by each subject, were permitted. No formal exercises, massage or physiotherapy was used. All subjects were told to continue their occupation and habitual degree of physical activity. The significant data on each patient are given in Table 4.

The predicted total weight loss for this group of 42 subjects was 786.7 pounds. The observed weight loss was 603 pounds, giving a performance index of 76.6. The average of the individual performance indexes was 78.8 with a standard error of the mean of 3.1.

The average weight loss per week was 1.90 pounds, and it varied from 1.00 pound per week (subject 1) to 3.17 pounds per week (subject 34). The performance index in these 2 subjects was 32.5 and 91.8 respectively. In these 2 subjects the performance index and the crude loss of weight per week are proportional. In other subjects this relationship does not necessarily follow. For example, subjects 12 and 37 each had a performance index of about 75 but their crude loss of weight per week was 1.5 and 2.5 pounds respectively. Subjects 36 and 9 each had a performance index of around 90 but a crude loss of weight per week of 1.6 and 2.5 pounds respectively. There was, therefore, no necessary correlation between the crude weight loss per week and the performance index.

The performance index of the 23 subjects who were less than 25 per cent overweight was 78.2 which is similar to the performance index of 78.8 for the entire group. There were 7 subjects who were more than 50 per cent over their ideal weight. Their performance index ranged from 32 to 116. In this small group of 7 subjects, the average of the performance indexes lacks significance.

The performance index of the 8 subjects who were given a 1500-calorie diet was 76.5, but

TABLE 4

SUMMARY OF DATA ON UNSELECTED GROUP OF 42 SUBJECTS USING CITRUS FRUIT AS AN ANOREXIC AGENT

SUBJECT	SEX	AGE	HEIGHT (INCHES)	ACTIVITY PER CENT (TABLE 1)	INITIAL WEIGHT (POUNDS)	IDEAL OR DESIRED WEIGHT (POUNDS)	POUNDS OVERWEIGHT	PER CENT OVERWEIGHT	PREDICTED BASAL CALORIES	PREDICTED TOTAL CALORIE EXPENDITURE	PRESCRIBED DIET IN CALORIES	CALORIE DEFICIT	PREDICTED WEIGHT LOSS PER WEEK (POUNDS)	WEEKS OBSERVED	TOTAL PREDICTED WEIGHT LOSS (POUNDS)	OBSERVED TOTAL WEIGHT LOSS (POUNDS)	OBSERVED WEIGHT LOSS (POUNDS PER WEEK)	PERFORMANCE INDEX
1	F	23	66	50	205.00	134.00	71.00	52.99	1760	2640	1100	1540	3.08	8	24.64	8.00	1.00	32.5
2	M	62	70	40	197.25	184.00	13.25	7.20	1800	2520	1500	1020	2.04	10	20.40	13.25	1.32	64.9
3	M	39	66½	50	212.25	150.00	62.25	41.50	1870	2805	1500	1305	2.61	10	26.10	20.25	2.03	77.6
4	M	18	69	50	275.00	144.00	131.00	90.97	2450	3675	1500	2175	4.35	6	26.10	10.00	1.67	38.3
5	F	57	64½	50	181.00	146.00	35.00	23.97	1540	2310	1100	1210	2.42	9	21.78	20.00	2.22	91.8
6	F	35	62½	40	169.75	147.25	22.50	15.28	1530	2140	1100	1040	2.08	11	22.88	14.75	1.34	64.5
7	F	42	63¾	50	218.00	138.00	80.00	57.97	1700	2550	1100	1450	2.90	8	23.20	17.00	2.13	73.3
8	F	28	62¼	50	137.75	124.00	13.75	11.09	1420	2130	1100	1030	2.06	4	8.24	7.50	1.88	91.0
9	M	33	71	50	194.00	166.00	28.00	16.87	1920	2880	1500	1380	2.76	4	11.04	10.00	2.50	90.6
10	F	47	65¾	50	204.50	137.00	67.50	49.27	1680	2520	1100	1420	2.84	5	14.20	8.50	1.70	59.9
11	F	58	63	40	194.50	127.00	67.50	53.45	1540	2160	1100	1060	2.12	5	10.60	10.00	2.00	94.3
12	F	53	62½	50	159.00	125.00	34.00	27.20	1420	2130	1100	1030	2.06	4	8.24	6.00	1.50	72.8
13	F	34	60½	50	163.50	121.00	42.50	35.12	1480	2220	1100	1120	2.24	10	22.40	14.00	1.40	62.5
14	F	41	63¼	50	206.00	137.00	69.00	50.36	1660	2320	1100	1220	2.44	10	24.40	20.50	2.05	84.0
15	F	28	62¼	50	147.25	124.00	23.25	18.75	1470	2205	1100	1105	2.21	6	13.26	8.50	1.41	64.1
16	F	32	65¾	50	196.00	137.00	59.00	43.07	1680	2520	1100	1420	2.84	4	11.36	11.50	2.88	101.2
17	F	36	63½	50	148.50	129.00	19.50	15.12	1460	2190	1100	1090	2.18	10	21.80	15.50	1.55	71.1
18	F	32	65½	50	197.00	136.00	61.00	44.85	1680	2520	1100	1420	2.84	8	22.72	16.25	2.03	71.5
19	F	24	65½	50	143.00	132.00	11.00	8.33	1500	2250	1100	1150	2.30	9	20.70	11.50	1.28	55.6
20	F	18	65	50	159.00	142.50	16.50	11.58	1580	2370	1100	1270	2.54	5	12.70	14.75	2.95	116.1
21	F	36	61	50	161.00	122.00	39.00	31.97	1480	2220	1100	1120	2.24	8	17.92	10.50	1.31	58.6
22	F	45	58	50	155.25	127.25	28.00	22.00	1340	2010	1100	910	1.82	13	23.66	24.50	1.88	103.6
23	F	56	66¾	40	174.00	141.00	33.00	23.40	1620	2270	1100	1170	2.34	6	14.04	7.25	1.21	51.6
24	F	42	62½	40	173.75	141.50	32.25	22.79	1520	2120	1100	1020	2.04	12	24.48	21.75	1.81	88.8
25	F	50	63½	50	161.00	142.25	18.75	13.18	1440	2160	1300	860	1.72	10	17.20	18.75	1.88	109.0
26	F	43	61½	40	171.25	144.00	27.25	18.92	1520	2120	1100	1020	2.04	12	24.48	20.50	1.71	83.7
27	F	21	66¾	50	174.25	145.00	29.25	20.52	1640	2460	1100	1360	2.72	9	24.48	15.50	1.72	63.3
28	F	29	63	50	143.00	131.00	12.00	9.16	1420	2130	1100	1030	2.06	6	12.36	12.00	2.00	97.1
29	F	40	60	50	163.00	132.00	31.00	23.48	1460	2190	1100	1090	2.18	11	23.98	23.75	2.16	99.0
30	F	20	66½	50	205.00	134.00	71.00	52.99	1760	2640	1100	1540	3.08	4	12.32	6.50	1.62	52.7
31	M	62	70½	50	215.50	180.00	35.00	19.44	1860	2790	1500	1290	2.58	10	25.80	22.00	2.20	85.3
32	M	45	69	50	188.75	176.75	12.00	6.79	1820	2730	1500	1230	2.46	5	12.30	12.00	2.40	97.6
33	F	30	63¼	50	150.50	129.00	21.50	16.67	1470	2205	1100	1105	2.21	4	8.84	9.50	2.38	107.5
34	M	26	70	50	232.00	180.00	52.00	28.89	2150	3225	1500	1725	3.45	6	20.70	19.00	3.17	91.8
35	F	20	65	50	162.75	130.00	32.75	25.19	1600	2400	1100	1300	2.60	5	13.00	10.25	2.05	78.8
36	F	60	60	50	148.25	125.00	23.25	18.60	1340	2010	1100	910	1.82	12	21.84	19.75	1.64	90.4
37	F	23	67¾	40	267.00	150.00	117.00	78.00	2000	2800	1100	1700	3.40	7	23.80	18.00	2.57	75.6
38	M	46	66½	50	173.00	160.00	13.00	8.13	1820	2730	1500	1230	2.46	8	19.68	13.00	1.63	66.1
39	F	44	56½	40	235.00	150.00	85.00	56.67	1620	2170	1100	1070	2.14	5	10.70	12.50	2.50	116.8
40	F	53	66¾	40	230.00	180.00	50.00	27.78	1840	2580	1100	1480	2.96	8	23.68	13.50	1.69	57.0
41	F	17	68	50	159.50	140.50	19.50	13.88	1680	2520	1100	1420	2.84	9	25.56	19.00	2.11	74.3
42	F	49	60	50	155.75	130.00	25.75	19.81	1440	2160	1100	1060	2.12	9	19.08	15.75	1.75	82.5

again this is too few subjects to determine whether or not more liberal diets give a better or worse performance index than is the case with an 1100-calorie diet.

DISCUSSION

THERE are several inherent errors in the individual performance index: (1) The standards used for calculating basal metabolism, which in normal subjects is a range usually considered about 10 to 15 per cent on either side of the average; this is unavoidable since most physiologic constants vary within a normal range. (2) The variable calorie value of a gram of adipose tissue due to variations in its water content; normally adipose tissue contains between 10 and 25 per cent water, which yields in metabolism from 7.0 to 8.4 calories per gram. In our calculations the water content of adipose tissue has been taken as 17 per cent, with each gram yielding in metabolism a constant 7.7 calories. (3) The normal variations in the proximate composition of the foods which varies considerably on either side of the averages which are used for calorie calculations. (4) The allowance for physical activity which must be more variable than the basal energy expenditure. Fortunately for our calculations most obese subjects fall into two occupational categories, housewives and sedentary workers. When obese, an allowance for activity in these subjects of 40 or 50 per cent of their basal calorie expenditure is usually the proper estimation.

With all these possible inherent errors one should expect considerable variations in the individual performance index. In subject C. D., the performance index varied from 101 to 119 in different periods while in our selected group of 11 subjects the variation was from 85 to 118. It is on this basis that we categorically accuse each subject of dietary errors whenever they fail to equal at least 85 per cent of prediction. Whenever they do better than 115 per cent of prediction we tell them they are losing excess fluid.

The errors inherent in the individual performance index tend to balance each other in the group performance index if a sufficient number of subjects is studied. This is shown by the performance index of 100 in the selected group of 11 subjects with a standard error of the mean of 3.4.

We feel the group performance index method of comparing the effectiveness of various reducing regimens in groups of patients has many advantages over a simple comparison of the average crude weight loss per week. In the first place, it eliminates the necessity for matching the groups according to age, sex, height, weight, basal metabolism and physical activity. This matched pair technic has proved so difficult that it is usually not attempted in groups of obese subjects. Furthermore the performance index gives quantitativeness to the result, so that effectiveness of management can be compared even when diets of widely varying sub-calorie values are used. In addition, people of both sexes with varying ages, heights, degrees of overweight and of physical activity can be included in the same group.

The results, when expressed as the performance index, really represent the degree of adherence to the prescribed diet—for groups of people, if they adhere to the prescribed diet and regimen, will give an index of 100, plus or minus a reasonable degree of error.

The use of about 50 calories of citrus fruit taken in the late morning and afternoon 30 to 60 minutes before the next meal has very definite advantages as an anorexic agent. Most people like it. It is readily available in homes either fresh, canned, or concentrated and frozen or refrigerated. Practically every restaurant, lunch counter and soda fountain has it. It supplies about 10 to 15 gm. of readily available carbohydrate to combat hypoglycemia which may occasionally occur about that time. Its use at that time tends to prevent the subject from consuming foods high in calories. It also acts as an appetite appeaser without providing a large number of calories. This is shown by a group performance index of 78 which represents, we believe, a high degree of adherence to the prescribed regimen.

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Management and Treatment of Cosmetic Dermatitis

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DERMATITIS caused by allergy to cosmetics, considering their widespread use, is not common. Improved methods of manufacture and clinical research before products are released to the public have greatly reduced the number of cases of this condition seen by dermatologists.

Most cases of cosmetic dermatitis that we see today in men and women are caused by new products which often contain skin sensitizers. The physician should be wary of accepting the patient's statement that the eruption is caused by cosmetics. Very often patients will regard rosacea, toxic erythemas, seborrheic dermatitis and staphylococcic folliculitis as cosmetic dermatoses.

Both sexes may be subject to this condition. Products which may cause sensitization include: hair dyes, hair tonics, waving solutions, lipstick, nail polish, base coats, freckle creams, hair lacquer and shaving lotions.

Various creams may cause allergies if they contain essential oils, estrogens or wetting agents.

CAUSES OF COSMETIC DERMATITIS

(A) *On the part of the patient:*

1. The directions of the manufacturer are not followed.
2. The cosmetic is used on an irritated skin.
3. The cosmetic is applied too frequently or vigorously.
4. The area on which the cosmetic is applied is exposed to excessive sunlight. Photosensitization in lipstick cheilitis is not always a factor according to Zakon.[1] Only 4 of his 32 cases (12.5 per cent) experienced their first symptoms in the summer.

(B) *On the part of the cosmetic:*

1. The cosmetic may have deteriorated due to age, action of light or poor storage facilities.
2. The cosmetic may be unstable due to absence of stabilizers or emulsifiers.
3. The cosmetic may contain potential sensitizers.
4. Cross-sensitization may be present to penicillin, sulfonamides, local anesthetics, etc.
5. The cosmetic may undergo chemical changes resulting in the production of secondary irritating substances.
6. The cosmetic may be contaminated by minute amounts of powerful sensitizers (nail polish, dyes, etc.) as suggested by Leider and Furman.[2]

(C) *On the part of the manufacturer:*

1. The manufacturer may release a product without proper clinical research over a long period of time.
2. He may use substitutes for safer products because of cheaper price, or unavailability.

The popularity of aerosol sprays, containing deodorants, cologne, or leg make-up, may produce a large number of cases of dermatitis in sensitive individuals, due to the fact that these preparations contain wetting agents which permit greater penetration.

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DIAGNOSIS

The recognition of skin disorders due to cosmetic sensitization may be very simple or very difficult. The obvious cases are those caused, for example, by cuticle removers or depilatories. Difficult cases are those in which the eruption is more or less nonspecific. Various factors, such as sun or windburn, nervous upsets, dietary indiscretion, occupational and domestic contactants must also be considered in the differential diagnosis.

In many cases, but not in all, the eruption usually follows within 24 to 48 hours after use of a new cosmetic. Patch testing as an aid in the diagnosis of these cases is not as useful as one might expect, and this is not done in the orthodox fashion.

Since the factors of evaporation, friction and photosensitization often play a part, the orthodox patch test is not satisfactory. I usually advise patients to re-apply the suspected cosmetic on the affected site, after the eruption has disappeared, in order to prove to myself that the cosmetic was really the cause of the dermatitis.

It is important not to be swayed too much by the voluntary suggestions of the patient as to the cause of the dermatitis. One must be open-minded in analyzing each case, and not condemn a cosmetic unfairly unless there is definite proof.

The six rules for diagnosing a cosmetic eruption are:

1. History in most cases of the eruption appearing within 24 hours after the use of a new cosmetic.
2. The eruption must first appear at the site of the application of the cosmetic (except in nail polish dermatitis).
3. The morphology of the eruption must fit in clinically with contact dermatitis.
4. The eruption should clear up within a week after discontinuing the suspected cosmetic.
5. The eruption should reappear following use of the suspected cosmetic on the same site.
6. Patch tests using the cosmetic and applied by the physician on or near the affected site may corroborate the diagnosis.

PROGNOSIS

These eruptions usually clear up within a few days to one week, except in the hair dye cases, where there is a great deal of inflammatory reaction, toxic absorption and a disturbance of the blood and liver function. In these cases hospitalization is advisable in order to avoid permanent loss of hair, secondary infection and involvement of the eyes. Onychosis as a result of base coat sensitization usually requires three months to clear up.

TREATMENT

THERAPY should consist of common sense plus the mildest of treatment, depending upon the extent of the pathology. After discontinuing all cosmetics temporarily, boric acid or aluminum acetate wet packs should be used in the edematous cases, and a zinc oxide-starch lotion applied in the erythematous cases. Ointments should be avoided in the acute eruptions.

Since cosmetics are a practical necessity, a hypo-allergenic or a specially formulated preparation should be prescribed as a substitute for the suspected product. Direct testing with the ingredients of the cosmetic used by the patient may reveal the irritant which may be the perfume, dye, resin, plasticizer, lanolin, etc. Testing sets prepared by some of the manufacturers of hypo-allergenic cosmetics can be obtained by the physician and patch tests made in an attempt to discover the sensitizing ingredient.

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COMING POSTGRADUATE COURSES

University of Minnesota Medical School, Minneapolis
Continuation course in pediatrics, March 26-28, at the Center for Continuation Study. Course is intended for general physicians and will be devoted to infectious diseases and common orthopedic problems in infants and children. Visiting faculty members will be Dr. Ralph V. Platou, New Orleans and Dr. William L. Bradford, Rochester, N. Y.

Course in fractures and surgery of trauma, for general physicians and surgeons, March 1-3, at the Center for Continuation Study. Dr. Carl E. Badgley, University of Michigan, will be the visiting faculty member and will present the annual Clarence M. Jackson Lecture

American Academy of Forensic Sciences, Chicago
Annual meeting, March 1-3, at Drake Hotel, Chicago

Diagnostic Clinic

Cryptogenic Fever

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Labeling as "cryptogenic," those fevers whose etiology is obscure, the author presents diagnostic criteria for various conditions accompanied by fever which have been found to offer difficulties in diagnosis.

The connotation of the word "cryptogenic" is familiar to everyone. It has its origin from the word which signifies something hidden or at least obscure. For us, the expression "not obvious" fits the majority of conditions, for sooner or later practically all of the conditions no longer are secret or hidden.

The late Dr. Besley, whom some of you knew, said that the only one who could diagnose all cases correctly was a junior intern. As a teacher I would amend that to say that the only one who can correctly diagnose every case is a junior medical student—to him nothing is obscure. At times I have been astounded at the correctness of his diagnoses, even from the top row of a fair-sized amphitheater.

My first patient with a true cryptogenic fever proved to have an abscess of the right frontal lobe. The process remained cryptogenic until just before death, when an ocular palsy in this diabetic patient pointed the way to the location of the lesion. I passed a fine spinal needle through the supraorbital foramen and aspirated pus. I would not dare do such a thing today.

My second patient with a cryptogenic fever finally proved to have a carbuncle of the kidney. Some of you remember the late Dr. Louis Mix who pointed out to me a lesson which I have not forgotten: In the wake of a carbuncle or a boil and with a continued insidious fever, look for a metastatic staphylococcal infection—as, for example, in thrombosis of the cavernous sinus that we occasionally see following a staphylococcal infection elsewhere in the body.

Time was when pyelitis, pylephlebitis and otitis media were the foci of attack in obscure fever. Today all these conditions are recognized; obscurity has become obvious.

Our patient is an adult business man whom we will call Mr. Barton. That is not his true name; he has a distinguished old Dutch name. Mr. Barton decided to take a little trip; he went down into Indiana, where he stopped for a short period of time on his way to the Ozarks. While in Indiana he began to feel quite exhausted. He started toward the Ozarks but did not make it and returned to Chicago feeling feverish, exhausted, and finally collapsed on three different occasions. He was hospitalized and a diagnosis of an active duodenal ulcer was made, largely because of an anemia and a proved duodenal defect. Treatment did not produce any certain result.

We have, therefore, a patient who leaves Chicago, goes into a neighboring state, visits for a time, becomes ill, starts on another jaunt and returns to Chicago. With such a history, our

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attention is focused primarily on a condition which he could have picked up on his journey. The hole in the argument, however, is that the time interval was hardly such as to permit him to pick up anything except in its very early stages.

For purposes of teaching, let us assume that he actually made the trip. Immediately there comes to mind the typhoid-paratyphoid group and the allied bacillary infections. Here, however, our incubation period should have been longer and the onset more gradual. In Indiana there is an occasional malarial infection, but Mr. Barton had no actual chills, headache, nausea, vomiting or abdominal pain, or recurrent type of pyrexia; there was nothing which would make a diagnosis of malaria plausible. In Indiana there was at one time a locus of undulant fever, so that the diagnosis of undulant fever must be kept in mind.

I assume that such a patient as Mr. Barton would be given the usual blood counts, blood cultures, agglutination tests, blood smear test and all the usual laboratory tests. A leukopenia would point to the typhoidal group, to the undulant fever group or to malaria. If a leukopenia were present at this stage I think a tentative diagnosis of at least one of these three conditions should be made. A normal sedimentation rate would help support the likelihood of undulant fever, even before the results of the other tests were known. I point that out to you, that if the sedimentation rate in a patient with obscure fever is entirely normal and if the history of undulant fever is reasonably plausible, you may arrive at such a tentative diagnosis on that basis alone.

Our patient returned to Chicago, and nothing fitted into this diagnosis. He had a fever and a rapid pulse, but he had a leukocytosis and completely negative agglutination tests. But he did have a splenomegaly.

By the time he got to us, which was almost three months after his fever had started, he was still on his feet, but staggering. He looked pale, washed out, was running a fever and had a rapid pulse. The rapid pulse does not fit in, of course, with the typhoidal group or with a similar allied bacillary infection. He had a very definite anemia. There was a slight swelling beneath the eyes and some edema of the feet. The liver was readily palpable and the spleen, as I have already noted, was palpable. With such a picture, the diagnosis of a septic state is obvious.

What was this obscure fever? What was the etiology of what I am terming a cryptogenic infection? This infection was not cryptogenic at all. All the signs and symptoms pointed to a coccal infection as opposed to an infection with a bacillary type of organism.

On the second day of observation he accommodated us with a small petechia under his finger nail. Going back into the patient's history, he had had rheumatic fever and he showed all the characteristic findings of a mitral stenosis. In such a patient, the likelihood of subacute bacterial endocarditis is very high. Blood cultures may not be positive, but with a mitral heart, murmurs, tachycardia, leukocytosis and fever, whether you have a positive culture or not, you may proceed at least to classify the patient as one with subacute bacterial endocarditis.

So we have a patient who goes on a trip, gets sick while on the trip, collapses, faints two or three times, is finally brought back to Chicago, continues to run a fever, has a known duodenal ulcer, presents the picture of an anemia, which instantly focuses attention on the likelihood of a hemorrhage to support the findings of the anemia.

However, he has a history of rheumatic fever and he has a mitral stenosis, so that our first diagnosis in Mr. Barton is and should be that of a subacute bacterial endocarditis, and it remains for us to isolate the organism.

THE first procedure in a patient of this type is to obtain a blood culture, and not a blood culture in one medium, but a culture in more than one medium, and not one culture, but more than one. Antibiotics should not be given before the culture is taken because they attenuate the organism, alter the fertility of the organism and may make it impossible to recover the organism. The antibiotics can be given after one or two blood cultures have been made.

I would like to call your attention to another thing. In pernicious anemia and other severe anemias, too often we give liver, and in doing so we rapidly convert the bone marrow into such a state that it is no longer possible to completely diagnose a macrocytic or pernicious anemia. Consequently if we start giving our patient liver and he happens to have pernicious anemia, we may pass up the value of the sternal puncture because of the changes which occur in the bone marrow after such an injection. In all

severe anemias, if you are going to give liver, give it after you have done your sternal puncture. Incidentally, sternal puncture is becoming much more important and will be used much more than in the past.

So also with the reticulocyte count where you are trying to establish an etiology for the anemia. Get your reticulocyte count first, or a couple of reticulocyte counts, and then when you give liver watch for the reticulocyte increase on the fourth or fifth day, which may cinch a diagnosis of macrocytic anemia.

Mr. Barton did have a *Streptococcus viridans* infection. He had a typical subacute bacterial endocarditis. The blood culture was positive in large numbers. He received penicillin in too small doses for some time. Finally he was put on continuous intravenous medication of a million units a day with intramuscular injections also, and finally 600,000 units per day. The blood stream was completely free of organisms and has remained so for a long period of time.

He has, then, all of the findings of mitral stenosis, a history of rheumatic fever, a systolic and diastolic murmur at the apex, and a soft systolic murmur at the base, secondary involvement, or perhaps we should say that he has a double lesion and he had petechiae. He had this obscure fever, but he was about three months trying to find out what it was all about. So once more I go back—that when you have a mitral lesion or an aortic lesion of definite rheumatic type and the patient begins to run a fever, you have endocarditis in the majority of cases, positive blood culture or not.

I have mentioned the patient with a brain abscess who came to me early in my experience and was diagnosed just before St. Peter grasped him by the hand.

I don't believe that nowadays otitis media, sinusitis, septic throat, cervical Hodgkin's disease, cervical tuberculous adenitis or ordinary tuberculosis is difficult to diagnose. Occasionally a miliary tuberculosis will be confusing, particularly when it is seen late in the picture and when it is part of a terminal state. But remember that an active tuberculous lesion anywhere in the body and an obscure fever predicate the possibility of miliary tuberculosis, particularly in the genital tract in the male where we may neglect to look for it, less often in the genital tract in the female, and of course, commonly in tuberculous lesions in the lung. If you have a tuberculous lesion and the patient begins to run a fever and the fever is obscure, the likelihood is of a miliary tuberculosis.

LUNG ABSCESS

What have been the cases which have bothered me, confused me, and turned up at autopsy with the wrong diagnosis? Starting toward the top of the body, I believe I would first mention abscesses of the lung, small abscesses, particularly when they are behind a bronchogenic carcinoma, i.e., a small papillary carcinoma of a bronchial tube, with a blocked tube, then a small abscess behind this point, with an obscure fever which may terminate with a large abscess, a carcinomatous spread or both.

BRONCHIECTASIS

Bronchiectasis may also be confusing. Incidentally, bronchoscopy will be used more frequently in the future. Bronchograms are part of the diagnosis of any obscure pulmonary state. They are relatively easy to do and they do not provoke much reaction in the average patient. In any suspicious lesion a bronchogram and, if necessary, bronchoscopy following the examination of several specimens of sputum, are entirely in order.

Theoretically we should see more bronchiectasis in the future if virus infections are to plague us as they have in the past. Those of you who recall the influenza epidemic of 1918 remember that the patients developed interstitial emphysema and bronchiectatic areas throughout the lung or pockets of localized bronchiectasis, and they complained of never having been well "since they got the 'flu.'" In the atypical pneumonias and virus infections that we have seen relatively recently, we have many patients of similar character. They feel rocky from the day that they get the infection. Look out for a small pocket of bronchiectasis in these patients.

CARCINOMA OF THE LUNG

Carcinoma of the lung is becoming very common and small carcinomas of the lung are being spotted quite early. Metastasis from carcinoma of the lung is extraordinarily rapid at times, so that from a tiny lesion hardly discernible by any technic, a metastasis to the spinal vertebra or cord coverings can produce a

paraplegia within 10 to 14 days. In sudden paraplegia in an individual who may be running an obscure fever, look out for carcinoma of the lung as the primary origin for this lesion.

An occasional flat abscess under the diaphragm has been picked up at autopsy in cases that we have diagnosed otherwise.

A low-grade fever is almost always present in carcinoma of the lung. Bronchograms are important; bronchoscopy will be done much more frequently. Bronchiectasis should be borne in mind, and abscesses will be found much too frequently.

Anemia is part of the picture of this infection, perhaps a cough, and possibly blood in the sputum, but at all times have a mindful eye on the possibility of a primary carcinoma.

LUPUS

Lupus is another condition which is coming into our field of diagnosis—lupus without lupus, that is lupus of the heart or general organs without lupus of the skin. In a case which we missed some time ago, the essential symptoms were fatigue, fever, exhaustion, tachycardia without any cause (the findings in the heart did not explain the tachycardia), and particularly a persistent and low leukopenia. The leukocyte count was 3000 and under. Every known test was done for all the typhoidal group, and nothing was found.

This patient also exhibited very marked increase in the respiratory rate, so that with an increase in the respiratory rate and a tachycardia and fever and exhaustion, and with rheumatoid symptoms in the hands and arms, and aches and pains like rheumatic fever, we should have jumped to the diagnosis of lupus, but we forgot all about lupus. At autopsy the patient showed a verrucous endocarditis with a typical distribution of the vegetations which were hidden under a shelf; that is, they don't stick out quite so much as they do in ordinary rheumatic endocarditis. Lupus without lupus is a disease to bear in mind.

POLYARTERITIS NODOSA

Lupus is a part of the so-called collagen disease group. Instantly another member of the group comes to mind—polyarteritis nodosa. Here I can report on another case that came to the final accounting chamber without a diagnosis. When after long search no name can be attached to a condition, think of periarteritis or, as we prefer to call it now, polyarteritis nodosa with a bizarre picture, many organs involved, a low obscure fever, a little touch of nephritis, a few red cells in the urine, a diagnosis of rheumatoid arthritis, abdominal pain, nausea, vomiting, in fact every organ you can think of involved at some time.

In our patient, on opening the abdomen there were tortuous arteries studded with nodules, and a diagnosis was instantly made, but too late.

My suggestion is, biopsy suspicious areas at all times. I see no reason for not biopsying a lesion unless it is one in which hemorrhage might terminate the situation. The idea of not biopsying is absurd. Biopsy suspicious glands where they are present, the swollen vessels, the nodular vessels which are occasionally present; check the differential, and bear in mind that eosinophilia of relatively moderate degree in an obscure fever may very well be polyarteritis nodosa.

Polyarteritis nodosa accompanies many other conditions, and the primary diagnosis may obscure the polyarteritis nodosa. In a patient of Dr. Elliott's in Gary, Indiana, a carcinoma of the pancreas was diagnosed, and correctly diagnosed, but the patient had too much of a fever and other involvement, and at autopsy a polyarteritis was found.

In another case at the University of Illinois the patient had polyarteritis nodosa, but he also had polycythemia vera, as typical a case as one would ever see, but mixed up with this polyarteritis nodosa.

CARCINOMA OF THE PANCREAS

Carcinoma of the pancreas has been a very frequently missed lesion, particularly when it involves the tail of the pancreas. Fever, loss of weight, indigestion in the front, pain in the back, and early venous thrombosis of nodular character on both sides in the legs, sum up the picture of carcinoma of the tail of the pancreas quite commonly. With fever, loss of weight, nodular thrombosis, pain in the back and indigestion in the front, carcinoma of the tail of the pancreas should be suspected. Carcinomatous lesions of the pancreas are quite commonly associated with fever.

AMEBIC ABSCESS OF THE LIVER

I have naturally missed amebic abscess of the liver; so have you. I am not too sure at all times what part the amebae play in these obscure

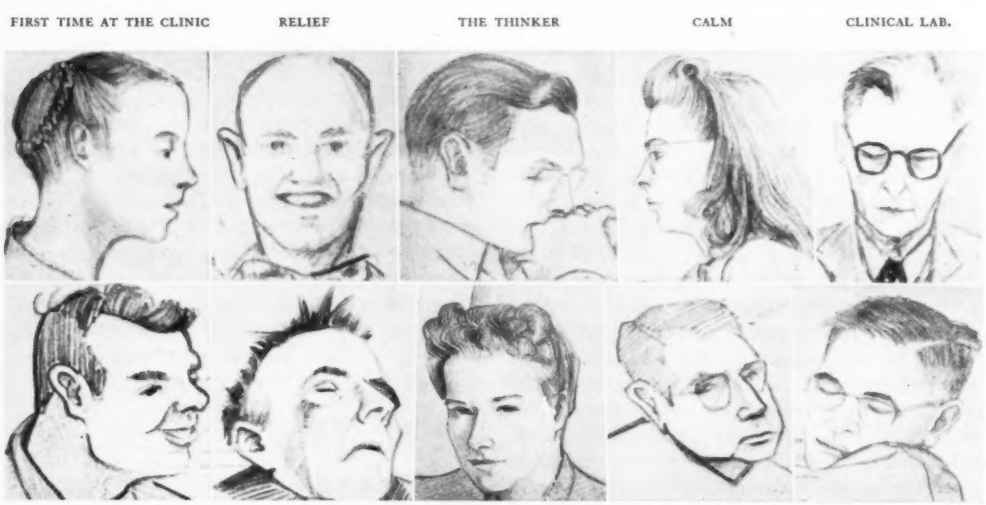
fevers. The patient should have adequate therapy. We have had cases of patients with amebae who terminated with completely other lesions in obscure fever. I would say that if the patient has amebae he should be subjected to therapy of some relatively benign type, at least for a time.

Malignancy will produce fever, and when malignancy metastasizes, fever becomes part of the picture.

The prostate is commonly involved in disturbances of malignant character, and prostatic malignancy metastasizes rapidly, not only to the glands in the region but all over the body. In certain of our cases of obscure fever the lesion has been primarily in the prostate.

We have one other patient who presents a picture also of an obscure fever. She has deformities in the hands, guttering of the dorsal muscles, nodulation on the fingers, rather definite atrophy of the thenar and hypothenar space—a picture of rheumatoid arthritis. This, however, does not concern us at present. The patient has come in because of a fever which she has had on four different occasions, and the etiology of her fever is not in the rheumatoid arthritis at all. It is due to a typical recurrent acute thyroiditis. She has complained of disturbance in her speech, which is due to some impingement on the recurrent laryngeal nerve. She has complained of difficulty in swallowing with the recurrence of this thyroiditis.

In this patient with two lesions, the etiology of her fever is due entirely to this recurrent thyroiditis which has responded to penicillin in the past, but she has developed a penicillin sensitivity, so she is now on CHLOROMYCETIN.



"THE PATIENT AND THE PATIENT"

(By Thomas C. Stevenson, M.D., Menlo Park, California)

(Sketches shown at the 1950 American Physicians Art Association exhibit)

Diagnostic Clinic

The Management and Outlook of Coronary Disease

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The vast bulk of coronary disease encountered clinically is on an arteriosclerotic background. Now arteriosclerosis is a progressive situation. Accordingly, coronary disease, too—as a rule—is progressive and passes through various stages or degrees, to wit: The average human being first sustains his "angina of effort." Later, sometimes years later, he develops an acute occlusion with massive infarction. As he grows older, his pathology leads him clinically into the third phase, "chronic coronary insufficiency." Due to earlier diagnosis and more adequate management, the outlook for these individuals is increasingly good.

In evaluating our present status of knowledge on the very important subject of coronary disease, and comparing it with what we knew or thought we knew 6 or 12 years ago, we can ask ourselves whither are we going and whence have we come? What does it look like? What is the score? Let me say to you, as you already know, before I go into my subject at all, that it is still one of the most important terminal causes, if you will, of our going out of this world. Two out of five of us will leave this world via our coronary arteries.

Talking percentages is like taking a number out of a hat—percentages can be anything—but the vast bulk of coronary disease, maybe 90 per cent of all coronary disease as I see it as a cardiologist and as you see it in general practice or in your various specialties, is due to arteriosclerosis, and that is the type I am going to discuss and which is exemplified by the patient I will present.

What is the other 10 per cent made up of? First, syphilis produces some clinical pictures of coronary disease, with the pouching of the intima of the aorta into the coronary mouths, thereby creating that typical pain or distress up the chest into the jaws or teeth or down the left arm which you and I recognize as the coronary syndrome. Syphilis does that, but syphilis is rapidly disappearing from the face of the earth, at least from the face of America, and the reasons for that, too, are sundry and too varied for me to go into. So we do not see much syphilitic heart disease any more; we see some and it can be confused with arteriosclerotic coronary disease.

We see the embolic types, but not many.

There is a third type which gives rise to the clinical picture of coronary disease, and closely resembles arteriosclerotic coronary disease, both clinically and from an electrocardiographic standpoint, that is, hypertension. You all see hypertensives who carry a very high blood pressure, both systolic and diastolic, and who because of that continuous pounding of their blood pressure upon their aortic ring near which the coronary mouths lie, develop that typical coronary pain referred into the neck and the jaws and the arms; they have T-wave inversions (I don't mind putting myself on record as saying that), in standard leads I and II, just as do our coronary arteriosclerotic patients. So the hypertensives can be very confusing.

But I am here to talk to you about the majority, the 90 per cent, of people with coronary disease due to arteriosclerosis. What is new on that subject which I should tell you? In the first place, males predominate. How much? Percentages vary with different cardiologists, but males predominate over females. I would

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ROBERT S. BERGHOFF

say roughly that I see 10 to 12 men to each woman with coronary thrombosis. Why is that? Again, when you ask why, you get onto theoretical ground and you have to do a little guessing—scientific guessing, but you are guessing just the same. I think probably the most plausible reason or explanation why we men develop, and die of, coronary disease much more frequently than do women, is because the intima of our coronary artery is, from birth all through life, much thicker than is the intima of the coronary of the female, and that increased thickness is due to its increased cholesterol content. This means that the male's coronary artery is more vulnerable for softening when he gets older and for the implantation upon that softened area of a thrombus than is the female's.

The second reason is still being written into the literature by cardiologists all over the country, that males lead a more strenuous life. I wonder. In this crazy, complex world the women are clipping it off pretty fast nowadays too. I think you had better take my first reason as the better one of the two. So much for the sex.

What age? Any age from 30 to 90.

Is coronary disease more frequent than it used to be? Surely it is, both actually and relatively. *Actually* it is much more frequent, because we are all getting very much older. As I look over this audience I say to myself, if you miss a few things like accidents from automobiles and a few other diseases, at least half of you will get to be 80 and 85 and 90 years old; whether you like it or not, you are going to be very old. So coronary disease is actually much more frequent than it used to be; there are more old people alive today than there were 10 or 20 years ago. Relatively is it on the increase? That is an important question. Some of my friends in the East think it is not. I think it is. Why? I don't know the answer to that except that the world is more complex. I find it more difficult to live today in every way than I did 20 years ago. People aren't as friendly any more; the world isn't as friendly; we have more to worry about. Anyway, there is more coronary disease. Put that one down for sure.

WHICH coronary artery is more frequently involved, the left or right? That has more than academic interest; it has real diagnostic and therapeutic interest. The left is more frequently involved with a thrombus than the right, but I will specify and modify that and say that vastly more people between the ages of 30 and 60 who develop coronary thrombosis have a thrombus in the left coronary artery than in the right. Why? There comes the old "why" again. That means guessing. Well, I suppose because between the ages of 30 and 60 in a man (and we are talking about men since they predominate 10 or 12 to 1 over women), the left heart does more work than the right heart. He is a busy guy, so his left coronary, which has to bring more blood to that active left ventricle, is overworked and that is where he gets his thrombus. The reverse is true, too. In the older decades of life past 60, the right coronary artery is more frequently thrombosed than is the left. Men get to be 70, 80, 90 years old and are either chairridden or bedridden and the left ventricle isn't working very hard any more, but the right one is because they develop bronchitis, bronchiectasis and all the things that go with old age.

We were saying that 90 per cent of coronary disease is due to arteriosclerosis. We become arteriosclerotic the day we are born and continue until we die. It is a progressive situation. The pathology is progressive, and if the pathology is progressive we have to pass through varying stages of coronary disease—we don't

have to, but at least 50 per cent of all people do. I have insisted upon that for 20 or 25 years and I still feel the same way. Not everybody has to have three stages of coronary disease, but half of the patients I see (and for 25 years I have seen nothing but cardiac patients) pass through the three stages. My anonymous great friend, to whom I am so grateful for coming here, has passed through three stages. What are they, and what is his outlook? What do we do for him? How do we diagnose it?

The first stage is the so-called stage of angina of effort. Just six short years ago I stood before this assembly and said, "The first stage of coronary disease due to arteriosclerosis is angina of effort, and we believe that it may be due to a spasm of the coronary vessel." Well, we have made a little progress there. We know that's out. In the first stage of coronary disease, where an individual has so-called angina of effort—where a person, after physical overstrain, emotion, excitement or fatigue, suddenly develops a severe substernal pain or distress which radiates into his jaws, his teeth, or down one arm or both, is of momentary duration, is relieved by postural rest or nitroglycerin or aminophylline or amyl nitrite—if that individual has a half dozen attacks like that he is not having a spasm of his coronary arteries at all; he has had a small infarction. That is important. We did not know that six years ago. We know it now. We have proved it time after time. You know how we have proved it. We have proved it by autopsy.

Since we know that an individual who has had a half dozen or more repeated attacks of angina of effort is having or has had those attacks, not due to a spasm of his coronary vessels but due to a closure of a small twig of the left or right artery, and because of that closure there is a small infarction, what shall we do with him? We are going to give him years of life; we are going to put him into bed, preferably in a hospital; we are going to treat him for that mild infarction; we are going to give him DICUMAROL; we are going to treat him just as we treat a massive infarction which he may get as his secondary stage.

ANGINA of effort is, therefore, the first and earliest stage of coronary disease due to arteriosclerosis. It is treated now, however, as though there has been no spasm of the coronary vessels but an infarction. All right, T. W. A. had his angina of effort for six whole months in 1945. He was not my patient then. He was given nitroglycerin and what-not and he got along pretty well. Then in 1946, he had what I am now going to describe to you as the secondary stage of coronary disease, an acute coronary occlusion with massive infarction. The diagnosis of that, fortunately, is relatively simple. You can all make it and you all do make it all the time, but you have to make it awfully quick; you have to make a diagnosis of an acute coronary occlusion with a massive infarction just as soon as you can, because the mortality rate in that situation has come down terrifically in the last four or five years due to early diagnosis, first, and second, to dicumarization.

How do you know when a given individual has had an acute occlusion with a massive infarction? Such an individual, after physical effort or mental excitation, or while at rest—much like the individual with a smaller infarction which we used to call angina of effort—usually has a more severe pain; it lasts longer, it is referred typically, like that in angina of effort, to the jaws, the neck and the arms. But that individual is in shock, he is almost always terribly sick, he is cold, he is sweaty, and with a stethoscope you find his heart tones are terrible, or without a stethoscope you find his radial pulse is fast and very irregular or very slow; he has had a block. You can look at that man and say, That fellow is really in trouble. He knows it, too. This is your so-called secondary stage of coronary disease due to arteriosclerosis—an acute coronary occlusion with a massive infarction.

What do we do for him? As many as possible of these people should be put into a hospital, if that is at all feasible, as soon as the diagnosis is made. They must have absolute physical, mental and emotional rest, which means sedation—I don't care what type, but usually you are safer if, for the first week, you treat these people with a massive infarction with opium in some form or other, either straight morphine or PANTOPON or codeine, but at least give them plenty of it for the first week. After that if you want to use the barbiturates that is all right, but they need a quick diagnosis and absolute physical, mental and emotional rest.

You may think this next remark is facetious and irrelevant. It is not at all. It is very important. Those people who are desperately ill should be allowed to see their immediate families—if a man, his wife; if he has children, one

or two children, but not a few friends who will come in and say, "You look pretty good, because your friend who had that last week is dead already." That is important, I repeat. The first week or two after a massive infarction, the family should be allowed to see a patient to keep up his optimism. If ever a doctor has to be optimistic with his patient it is then. You have to tell that man what he senses within himself—even if he doesn't sense it—"My friend, you are definitely going to get well." You have to tell him that! You have to reassure him. You have to exude a sense of optimism to that fellow who is fatally stricken: "You are going to make it, you are going to get well, and nothing else counts."

Absolute bed rest, emotional rest, mental rest, physical rest, soft bland food, proper but careful care of the bowels, and then as quickly as possible dicumarization. There is no question that dicumarol applied as early as possible and used to the point of bringing the prothrombin time down to 33 or even 30 per cent "bleeding time," in addition to other remedies I have already mentioned, has lowered the mortality rate of acute occlusion with massive infarction terrifically. Most of you are much younger than I, but you all remember that our mortality rate was 33 1/3 per cent, 35, 40, and we were desperately in need of help with these people. That mortality rate has come way down under that one adjunct, the anticoagulant.

That is the way to handle those people. You will say, "You haven't mentioned oxygen." Sure, if a man is at all dyspneic he needs oxygen, but if he isn't dyspneic at all I am not so sure that that should be a routine procedure. It has its drawbacks too. How are you going to give it to him—with a catheter in his nose? I don't want one in my nose unless I need it. With a mask that you have to fool around with? In a tent that gets clammily cold unless it is properly watched? Oxygen when it is necessary should be administered early and freely, but unless it is necessary it should not be used routinely.

THEN follows a period of rehabilitation after an acute occlusion with massive infarction, and that will take weeks. You may ask, "How long do you still keep a person in the hospital with an acute occlusion with massive infarction?" Well, that varies, doesn't it? It has to vary, but I am still old-fashioned enough to keep them there plenty long because they sustained an injury to the most vital organ in the body. There is only one heart in that body. It is not like the kidneys or lungs. They have a good-sized area put out of business, so it is a matter of weeks and weeks until clinically the patient feels well, until he reacts well to sitting up and walking around, until his electrocardiographic pattern also may have changed a bit, although that is no criterion—it may be fast and stay fast for a year. You have to gauge the duration of the stay of your patient in bed in the hospital upon his clinical situation and not his electrocardiographic tracing.

Given an individual, then, who has passed through his so-called angina of effort, who has weathered his acute occlusion with massive infarction, like my friend T. W. A., what happens then? Well, coronary pathology is progressive, arteriosclerosis is progressive, human life is progressive; we grow old the day we are born, but most of us are going to be very old people with or without coronary disease. What happens to a fellow like T. W. A.? Ah, life is rosy for T. W. A. He now has a chronic coronary insufficiency and he knows it. He knows that his coronary arteries are sclerosed, are narrower than mine, because he couldn't do what I am doing, probably. I could get mine while I am talking to you, but he would have some shortness of breath and distress while he was talking to you. I am getting more blood to my heart through my coronary arteries than an individual with coronary insufficiency, more than my pal here—T. W. A.

How do we handle those? Well, believe me, I am very optimistic about people who have had an acute occlusion with massive infarction if they are kept within their "energy potential," if they are told what they have had, if they are told how they shall live. Can they do much? Sure, they can do a lot. This fellow is an important fellow in the city of Chicago, but he knows that if he does certain things physically he gets pain, so he tries not to do them; he knows if he gets emotionally upset he gets distress, so he tries not to do that.

He is on drugs. What drugs for chronic coronary insufficiency? We all vary, we all have our hobbies, don't we? Every one of us has his own preferences in treating his patients. Papaverine is a good drug, there is no question about it. Maybe it is slightly habit forming, but not

too much. How much? A grain three times to six times a day over a long, long period of time.

Good old aminophylline. Fred Smith, long since gone, said from this platform one day that he would rather have aminophylline and no digitalis if he had to treat heart disease; he thought that much of aminophylline. I think it is a good drug. Papaverine and aminophylline are both used in the management of chronic coronary insufficiency.

Here is a point I want to make: How long can a man go on after he has had a massive infarction like T. W. A.'s, if he lives within his limitations? Is his life curtailed? He is about five years older than I am, I guess. He can live a long, long time. He not only can live a long, long time, but he can do what he is doing this morning. It is no fun to come down here and face all these people. It isn't simple, if you are not a doctor, even if you are a tycoon, to face all these doctors. But T. W. A. is all right, he won't have any trouble. Let's get down to a little more scientific basis and not be so facetious. T. W. A. is an ideal patient because he follows orders. He can eat pretty much what he wants. He knows he should never eat a big meal at night—nor should many of you—before he goes to bed. He knows he shouldn't get emotionally upset. He knows he shouldn't overdo physically.

Now we get to a few habits. Tobacco? I know full well that the country over cardiologists say once you have a coronary thrombosis, no tobacco. If the fellow has smoked all of his life, I say if he has no distress, and he is going to stay that way if he is careful, he can smoke in moderation. Alcohol? Oh, how I got myself in trouble in Milwaukee four years ago by making the following statement, which I make again. I do not advocate alcohol for a teetotaler, for a man who has never had a drink of whiskey. If a man has been a drinker and has had a coronary thrombosis, and if he is over 50 years old, a couple of drinks of whiskey a day is good medicine for that man. I am not advocating it for people who have not been drinkers.

THERE is one more subject that seems to be taboo but I will throw it at you, and then get off the stage. If the patient is married to a younger woman, you owe an obligation to your patient to say, "If sexual intercourse gives you pain, makes you breathless, no sexual intercourse, because it kills a lot of people." You can't lay down a blanket rule, but you as doctors have an obligation to inquire into that situation. A man will say to you, "My wife is twenty years younger than I am. What will I do?" Your answer, "Send her to me."

He sends his wife to you, and you say, "Are you twenty years younger than your husband?" You know she is not, but women are like that. So she is ten years younger. You say, "All right, that is a natural act, you are entitled to it, you want it, he wants it. He can't have it because the last time he tried that it almost killed him. Do you want sexual intercourse and a dead husband, or do you want no sexual intercourse and a live husband?" And a good woman always says, "It doesn't mean that much to me."

Diagnostic Clinic

Causes of Failure in the Surgical Treatment of Hypertension

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Causes of failure in surgical treatment of hypertension are discussed from the point of view of four factors: (1) psychic, (2) technical, (3) renal, and (4) adrenal. Optimal operative procedures are outlined and illustrative cases presented.

In discussing the causes of failure in the surgical treatment for hypertension, I should like first to show a patient who is here. This gentleman is 30 years old, and I am showing him because he belongs to a group of patients who, in our experience, definitely benefit from splanchnicectomy.

This patient apparently had a normal blood pressure up to 1943 when he was rejected by the Army because of a blood pressure of 172/92. Previous blood pressure readings had been taken—in 1941 for life insurance—at which time he was rejected, although he was not certain that it was because of a high blood pressure.

In 1937 he had an appendectomy. His blood pressure was taken at that time but nothing was said about its being abnormal.

He was asymptomatic from his hypertension, and this is an important point, because hypertension runs a course of several years before any symptoms develop.

Two years previous to admission to the Illinois Research and Educational Hospital, however, he began to tire easily, and fatigue, as you know, is one of the early signs of hypertension. He had no dyspnea, no decreased cardiac reserve. He also had headaches, fronto-occipital in character. These had been getting gradually worse. He had no other complaints, no renal symptoms, no visual disturbances, no cardiac symptoms, no history of albuminuria, no renal disease or any type of urinary tract infection.

His physical examination was entirely negative except for a soft systolic murmur at the apex, which was not transmitted, and disappeared after exercise. His blood pressure on admission was 158/100 in the left arm, 152/90 in the right. Pressures in the legs were somewhat higher, which, of course, is usual. His spine was negative, and he had good peripheral pulses.

I shall not go over his laboratory workup, which is rather extensive, except to say that everything was practically negative. Blood chemistry was negative; x-ray examination for size of the heart, for configuration of the heart, was negative; renal function studies showed a concentration up to 1.027 and dilution down to 1.002 after ingestion of water, and he showed a 40 per cent excretion of phenolsulfonphthalein in 30 minutes, which, as you know, is excellent.

The cold pressor test is interesting in that his blood pressure rose from 166/106 in 30 seconds to 204/126 mm. of mercury, which is a marked response or marked reactivity to cold.

On giving him ETAMON (tetraethylammonium chloride), which, as you know, is a sympatheticolytic drug, the blood pressure fell from 144/100

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to 120/80. This is again an excellent response, indicating that his peripheral vascular bed is flexible.

When he was given 9 gr. of sodium amytal the blood pressure again dropped from 142/94 (you notice that his diastolic pressure is always close to 100, which is significant in a patient who is 30 years of age) to 94/72 mm. of mercury while he was asleep.

In the evaluation of this patient we felt that he had a mild hypertension from which he had sustained no significant renal damage, but his casual blood pressure, by which we mean the blood pressure which we can obtain during the day, at work, was always around 100 mm. of diastolic pressure.

We feel that this is the ideal case for sympathectomy, and this is why I brought him around. We did a bilateral transthoracic lumbodorsal sympathectomy on him in two stages and followed him ever since that time; I am not showing him because of late results, but because he is an ideal case for selection.

All we can show on him now are his scars, in which you might be interested.

These operations are transthoracic but intercostal, by which I mean that no rib is resected; the incision is made between the sixth and seventh or seventh and eighth ribs, and of course the pleural cavity is drained for 48 hours to get rid of the pleural exudate which always forms.

This operation is tolerated very well, but of course it has to be done in two stages about two weeks apart, and this is the maximal procedure that we are now doing in young, comparatively benign hypertensives.

A little later I shall discuss another procedure which we do in a different type of case.

Emphasis of the failure of any method of treatment does not mean dissatisfaction with it; on the contrary, it means an effort to eliminate *procedures* which are ineffective or *patients* who are poorly selected. The present report is based on the study of more than 400 patients who underwent surgery for hypertension. The causes of failure will be discussed under four headings, i.e., the psychic factor, technical factor, renal factor and adrenal factor. Before these factors are discussed in detail, I wish to present in tabulated form the indications which have been used for many years in selecting cases for operation and to state that with some modifications to be discussed in this paper, they have not changed during the course of years (Table 1).

GEZA DE TAKATS

TABLE 1

THE THREE GROUPS OF ESSENTIAL HYPERTENSION

GROUP 1 . . . Age below 40. Minimal or no detectable organic damage. Normal blood pressure on complete rest or barbiturates. Casual diastolic pressure above 100 mm. of mercury.

GROUP 2 . . . Age from 20 to 55. Moderate vascular sclerosis in all organs. Well demonstrable angiospasm. Diastolic pressure cannot be lowered below 110 mm. of mercury by any method. Rising diastolic pressure during the course of last six months.

GROUP 3 . . . Large recurrent retinal hemorrhage and exudates or papilledema. High fixed diastolic pressure, which cannot be lowered below 120 mm. of mercury. Congestive or anginal heart failure. Poor renal function. Numerous cerebrovascular accidents. An actual malignant or premalignant state of hypertension with continuous maximal angiospasm uninfluenced by either pressor or depressor stimuli.

From DE TAKATS, G., JULIAN, O. C. and FOWLER, E. F.[5]

ONE notes that early hypertension responds most favorably, but this should not lead one to operate too early. Adolescent hypertension can be watched and has been seen to subside; whether it will recur in the thirties during periods of stress cannot be determined in our material statistically; most clinicians, however, err on the other side and withhold the indication to operate until irreversible changes pre-

TABLE 2

PSYCHIC FACTOR IN HYPERTENSION

CASE	AGE	KNOWN DURATION OF HYPERTENSION, YEARS	GRADE OF HYPERTENSION	DISPOSAL	RESULT
1 (N. C.)	42	10	2	Unilateral sympathectomy	Postoperative psychosis State hospital
2 (L. C.)	37	7	2	Preoperative psychotherapy Bilateral splanchnicectomy Acute anxiety state Postoperative psychotherapy	Good result
3 (M. W.)	34	6	2	Bilateral splanchnicectomy	Hypertension markedly reduced Drug addiction?
4 (E. B.)	50	10	3	No operation Refused psychotherapy	Unknown

dominate. This presupposes a steady evolution of essential hypertension for which we have enough evidence in some of our own patients, who were advised operation, but who delayed it for months or years.

THE PSYCHIC FACTOR

Result of any surgical procedure can be vitiated by the patient's state of mind, but in hypertension where the central, neurogenic element is frequently a factor, and in which organic cerebrovascular lesions may produce identical phenomena with functional changes, more than the usual care must be exercised to exclude certain patients from operation or at least postpone the procedure until a better readjustment to their environment may be accomplished. Binger and his associates[1] have drawn a composite picture of the type of personality encountered in essential hypertension: exaggerated dependent strivings, submissiveness which is coupled with stubbornness, feeling of weakness and defenselessness, suppression of hostility, fear of injury and emotional detachment. The authors emphasized that the neurotic manifestations and the hypertension are not necessarily causing each other, that the personality disorder and the vasomotor instability may actually be different aspects of the same pathologic process.

CASE REPORTS

In this group of patients, some stand out as representing our changing attitude toward their surgical management (Table 2).

Case 1—This patient had never been known to have been in a mental institution before admission to the hospital, nor was this fact ever mentioned by her relatives. She was cheerful, cooperative, almost suspiciously eager to have a sympathectomy. Following the first stage she developed a severe manic-depressive psychosis, had to be transferred to a closed floor and finally to the Elgin State Hospital. Her hypertension, which was not too advanced, was of course unaffected. It then became known that she had been in a mental institution before.

Case 2—A psychiatrist referred this patient to us because of a severe progressive hypertension. After a month of preoperative psychotherapy, a two-stage splanchnicectomy was performed. In spite of continuous contact with the psychotherapist she developed an acute anxiety state, had to be transferred to a closed floor, but recovered from her acute anxiety and is said to be well adjusted with a casual blood pressure of 160/110 mm. of mercury as contrasted to a preoperative level of 230/150 mm. of mercury.

Case 3—The patient was a highly intelligent, high-strung woman of 34, whose 10 spells of unconsciousness in the last six years, followed at one time by a unilateral paresis of arm and leg, were interpreted by us as being due to transitory cerebrovascular accidents. She was also known to have a positive Wassermann reaction, for which she had received antiluetic therapy. Following a two-stage sympathectomy she assumed a completely negativistic attitude, consumed increasing amounts of narcotics and became bedridden. Both she and her husband refused psychotherapy and her further course is unknown. Recently she was admitted for a medical study and exhibited drug addiction.

Case 4—This patient was a 50-year-old woman with a severe progressive type of hypertension bordering on operability. She was screened by our neuropsychiatric resident and it was recommended that she submit to psychiatric care, although it was explained to her husband—30 years her senior—that operation could not be deferred for too long, because of the extensive organic damage. They refused both suggestions and have not been heard from since.

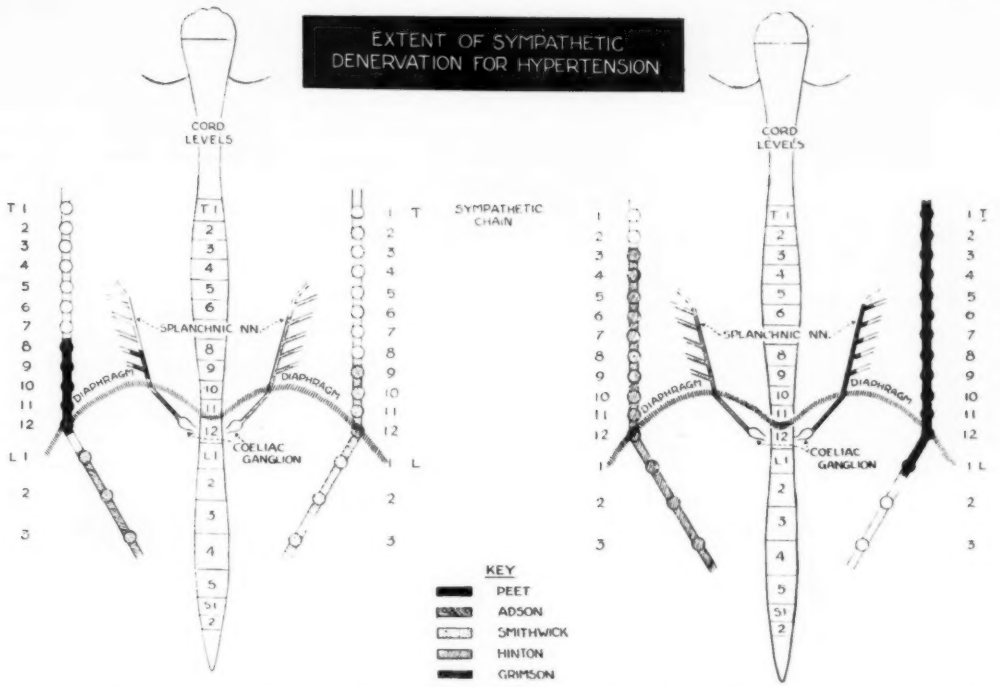

FIGURE 1. Extent of sympathetic denervation for hypertension. At present only two methods are used in my clinic, namely Smithwick's (right side of first diagram) and Hinton's (left side of diagram). The second procedure, however, is done transpleurally with an approach through the seventh intercostal space.

(From de Takats, G., Julian, O. C. and Fowler, E. F.[5])

I HAVE picked these four examples from a group of others to emphasize the method of approach to this problem: When in the course of the initial examination or after the careful history there is anything to suggest a mental conflict or abnormal mental tension, the resident in neuropsychiatry is asked to interview the patient.* This interview has been of great help to us. If the patient is approached tactfully, he or she is glad to unburden himself and this in itself offers him some relief from tension. The resident recommends either subsequent interviews with the attending man, or simply registers the personality changes which may not be severe enough to contraindicate operation. For those patients in whom a severe psychoneurosis or psychosis has been discovered, preoperative psychotherapy, followed by immediate and late postoperative psychotherapy, is carried out as in case 2. Unfortunately, this is a long and expensive procedure. Simply to state, however, that the patient's mental status does not permit surgery means that her vascular status will progress to failure. Rapid pre- and postoperative therapy, as outlined recently by Alexander and French,[2] may be useful in such a situation. As stated previously,[3] we have not seen any lasting hypotensive effect from psychotherapy. The method seems to be helpful in the preoperative and postoperative management of a certain selected group of patients.

*Lately, a psychiatric social service worker has been added to evaluate this group of patients.

THE TECHNICAL FACTOR

In spite of the great variations in the technic of splanchnic section which were proposed during the evolution of this operation, no agreement exists as to optimal procedure. Our standpoint has been that a *minimal* and a *maximal* procedure need to be established, the first being a technic which does not allow further restriction, the second a technic which need not be extended any further to improve results. The

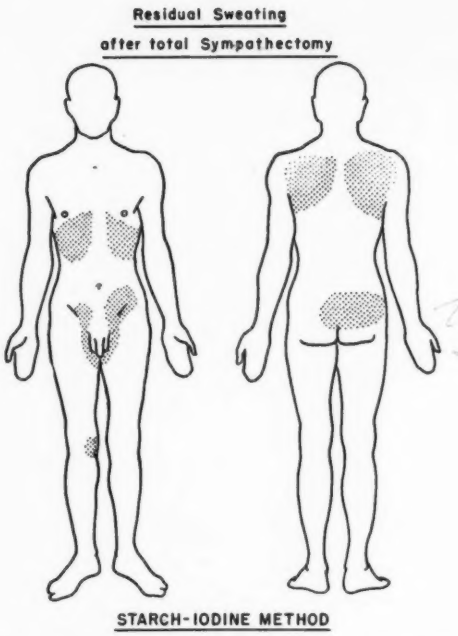

FIGURE 2. Residual sweating determined by the starch-iodine method. Patient underwent a bilateral total sympathectomy from D_1 to L_4, in four stages. Sweating test done two weeks after last stage did not seem to indicate regeneration but rather persistence of sympathetic activity.

diagram in Figure 1 indicates the various technics. Before 1940, this clinic used the supradiaphragmatic approach, the first time in 1932.[4] After 1940 the Smithwick procedure was used in the majority of patients, but the operation was extended cephalad in 1946 in advanced cases which were still acceptable for operation.

A control series of extensive total and subtotal sympathectomies has been started on the vascular surgical service at the Veterans Hospital; there has been no evidence so far that this group did any better than the one subjected to the minimal procedure.[5]

There is one exception, however. Young patients with rapidly advancing vascular disease or those in group 2 who are good surgical risks, have been subjected to a transpleural or extrapleural dorsolumbar sympathectomy, removing the sympathetic trunk from D_3 to L_2 on both sides. This is at present our *maximal procedure,* and nothing that I have seen in my own experience or in the literature would suggest the need for further extension of this procedure toward a total sympathectomy.

The danger of regeneration is, of course, always with us; since ganglia have now been recognized in the white rami and in the anterior roots[6] and since many of these must of necessity be left behind, the *longitudinal* extension of the operation seems unnecessary. Cushing clips placed tightly on cut ends have not been seen to permit growth of nerves distal to them. We are more impressed with the fact emphasized by Craig and Roth[7] that sympathetic fibers remain uncut within the area of intended denervation, and that sweating areas appear shortly after operation.

While it is far from my thoughts to minimize the technical aspects of the procedure and while our group has spent considerable effort in determining the optimal procedure, observations would indicate that the type of patient subjected to operation is far more important than the extent of the operation, provided, of course, that both major splanchnic nerves are cut. In the first place, a sweating around the waistline at the level of D_{12} to L_1 invariably develops months or years after operation without any bearing on the postoperative result.[8] I have frequently noted a very heavy ramus at L_1 or in the substance of the diaphragm which may well contain ganglia—they have been definitely recognized in the dorsal segment. Secondly, we have 10 patients in group 1 with excellent results, who sweat in one lower extremity and yet have exhibited normal blood pressures for periods extending from one to six years. Such patients may have to be reoperated on but certainly not before their blood pressure rises again. Even after total sympathectomy sweating areas make an early appearance (Figure 2).

THE RENAL FACTOR

IRREVERSIBLE cerebral, cardiac, renal or peripheral vascular damage vitiates surgical results and there is no further need to belabor this point. It seems, however, that the functional state of the kidney deserves special attention not only because hypertension per se gradually damages the kidney, but also because the damaged kidney may become a self-perpetuating factor in hypertension, since the fixed vascular and parenchymal damage in the kidney seems to be least capable of improvement. Compared with the improvement in the eye grounds, the size of the heart, or the electrocardiogram which follows

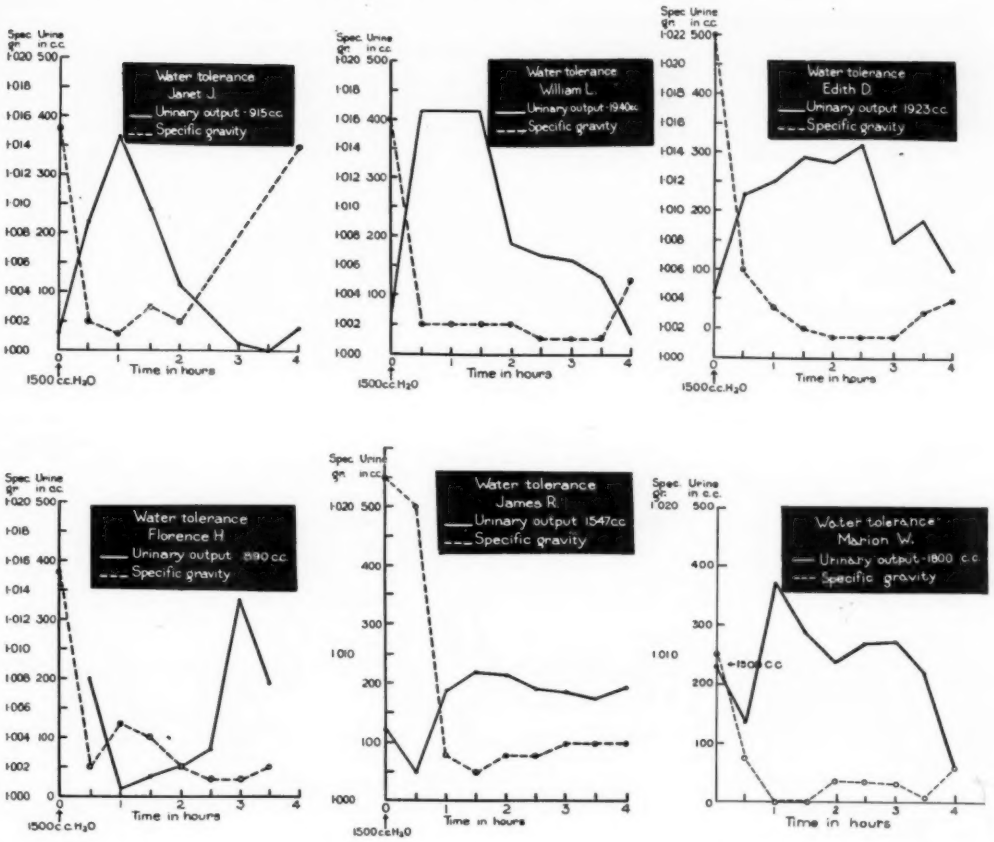

FIGURE 3. Decreasing adaptability of the kidney to handle 1500 cc. of water. Note that the water excretion is gradually delayed and that specific gravity remains low during the four-hour period. J. J., 42-year-old grade 1 hypertensive. Postoperative blood pressure (24 months' follow-up) 120/80 mm. of mercury. Complete relief of symptoms. W. L., 49-year-old grade 2 hypertensive. Blood pressure one year after operation 160/00 mm. of mercury. E. D., 30-year-old severe grade 2 hypertensive. Postoperative blood pressure (18 months' follow-up) 168/110 mm. of mercury. F. H., 52-year-old grade 3 hypertensive, postoperative blood pressure 190/110 after one year follow-up. J. R., fixed arteriosclerotic hypertension, 56 years old. Not regarded as a surgical case. M. W., 34-year-old woman, in impending renal failure, but no marked vascular damage elsewhere. Extensive splanchnicectomy failed to reduce her blood pressure.

splanchnicectomy, renal function seems to remain unchanged. Our usual clinical tests consist of a concentration-dilution test, the 15-minute phenolsulfonphthalein test and the urea clearance. The insulin-diodrast clearance has not proved feasible for the average hospital laboratory, although the recently simplified technic of Landowne and Alving seems to be of promise. We have used a simple water tolerance test instead of the customary concentration-dilution test and have been impressed by the information derived from it[9] (Figure 3).

It will be seen that starting from the normal curve, in which water excretion occurs early, and dilution later is followed by reconcentration in the four-hour period, there are all kinds of variations, in which the kidney is trying to compensate for its diminished concentrating ability by increasing urinary output. All these patients still show a wide margin between maximum concentration and dilution. On the opposite end of these patterns is that of M. W., who could only concentrate to 1.010, showed no sign of reconcentration and a larger output than intake.

TABLE 3

CORRELATION OF WATER TOLERANCE WITH RESULT OBTAINED BY DORSOLUMBAR SYMPATHECTOMY

PATTERN	NUMBER OF CASES	RESULT		
		Excellent	*Good*	*Failure*
1	15	13	2	
2	42	3	39	
3	29		21	8
4	9		1	8
5	No cases submitted to operation			
6	5		5	
TOTAL	100	16	68	16

In spite of a maximal resection of D_3 to L_3 bilaterally, she showed no response to splanchnicectomy.

Table 3 shows the correlation of the six patterns with results obtained after sympathectomy. An excellent result is a blood pressure below 140/90 mm. of mercury; a good result is a diastolic pressure stabilized between 100 to 110 mm. of mercury, when it was previously 130 to 150 mm. of mercury, and by failure I mean a blood pressure which has risen to the preoperative level—all these figures are based on a follow-up of at least one year. It will be noted that starting with the third pattern the number of good results give more and more room to failure and that excellent results were only obtained in the first two groups.

We have in the past rejected patients who failed to concentrate urine below 1.015 after 14 hours of water deprivation, or who showed a 15-minute P.S.P. excretion of less than 10 per cent of the dye or who had a urea clearance of less than 20 cc. per 100 cc. of blood.

In the present series, however, we encountered 16 failures, which did not fall into any of these categories. These operations were technically correct and the general vascular damage was not advanced. Essentially, these showed failure to reconcentrate urine in four hours together with a late excretion of water, the later, the more ominous. The water tolerance test has given us one more indication of irreversible renal damage. The group of 16 failures of patterns 3 and 4 showed a fair concentration-dilution test and would ordinarily be regarded as having sufficient renal reserve, since none of them showed less than 20 per cent excretion of the dye in 15 minutes and their urea clearance was not below 50 per cent of normal.

The normal water tolerance is defined as the ability of the individual to reconcentrate the urine in four hours* and to eliminate the ingested water mostly in the first two hours. It seemed to us that certain patterns signify irreversible renal damage or such extrarenal factors which sympathectomy does not influence. For this reason we have excluded from surgery patients with patterns 4 to 6, but are still observing recurrences or failures of operations done in other clinics.

TABLE 4

THE CORTICO-ADRENAL FACTOR IN HYPERTENSION
EXPERIMENTAL FINDINGS

Renal hypertension is decreased or abolished after bilateral adrenalectomy.

Hypertensinogen decreases in the blood after adrenalectomy and returns to normal on cortico-adrenal extracts.

The "General Adaptation Syndrome" includes cortico-adrenal stress and is often accompanied by hypertension.

Eosinophil preponderance in the pituitary trophic to the adrenal cortex produces diastolic hypertension.

Epinephrine or stimulation of the splanchnic nerve increases cortico-adrenal secretion.

TABLE 5

THE CORTICO-ADRENAL FACTOR IN HYPERTENSION
CLINICAL OBSERVATIONS

Hyperplasia or adenoma of adrenal cortex shows a higher incidence in hypertensives. (Reports to the contrary are available.)

Plasma electrolyte disturbance in the full-blown Cushing's syndrome is diametrically the opposite of that seen in Addison's disease.

Salt depletion is well tolerated in some hypertensives in contrast to normals.

Low sodium diet is effective in a group of hypertensives, acting through the adrenal cortex.

Desoxycorticosterone acetate produces a rise in blood pressure of hypertensives.

THE ADRENAL FACTOR

Cases of overlooked pheochromocytomas are sufficiently known, and this occurs not only in patients in whom the adrenal area is not exposed—as in supradiaphragmatic procedures—but also in instances where the chromaffin cell masses are grouped in atypical locations, such as around the aorta, at the iliac bifurcation and many other

*Lately, half-hour samples of urine have been collected for six hours to gain information on delayed reconcentration.

locations. In one case, studied on our service by Dr. John T. Reynolds and Dr. T. J. Coogan, the histamine response was useful, but this test is by no means specific and the recent introduction of benzodioxane has been of great help. This drug will only cause a fall in blood pressure when excessive epinephrine is present, and gives a small rise in essential hypertension.[10]

We have become more and more convinced of the necessity of thorough exploration of the adrenal gland during splanchnicectomy, in fact recommend it before any sympathectomy is undertaken. The gland should be inspected, palpated and measured, all the more since cortico-adrenal hypertrophies or adenomas are also potent and not infrequent factors in the production of hypertension.

There are several reasons why the investigation of the cortico-adrenal function in essential hypertension is of interest, and they are briefly summarized in Tables 4 and 5. The investigation of this factor may be done by tests which study the hormone output in the urine after administration of ACTH (adrenocorticotrophic hormone of the pituitary), by the diminution of lymphocytes or eosinophils after the use of the same hormone or after adrenalin and by tests relating to sodium retention. Our interest was to develop a simple clinical test to be run routinely on all patients for purposes of orientation; when this was found to point to cortico-adrenal activity other tests could be added.

I have marshalled evidence elsewhere to show that the insulin tolerance is a simple and clear-cut indication of pituitary-adrenal stimulation and this was the test employed in a series of 50 hypertensive patients, of whom 8 showed a complete resistance and 7 a partial resistance to insulin (Figure 4).

The analysis of the 8 patients is of great interest and has been published elsewhere.[11] Of these there were 2 males and 6 females. One male had a cortico-adrenal adenoma and the other was an insulin-resistant diabetic, who became insulin-sensitive after splanchnicectomy and now requires no insulin. The women fitted into the description of Schroeder's pseudo-Cushing's syndrome[12]—obese women with one or two but not all the characteristics of Cushing's syndrome. Such patients also show a diminished sugar tolerance and may show sodium retention. They are said to show a pressor response to desoxycorticosterone acetate, but I have not had any experience with this method.

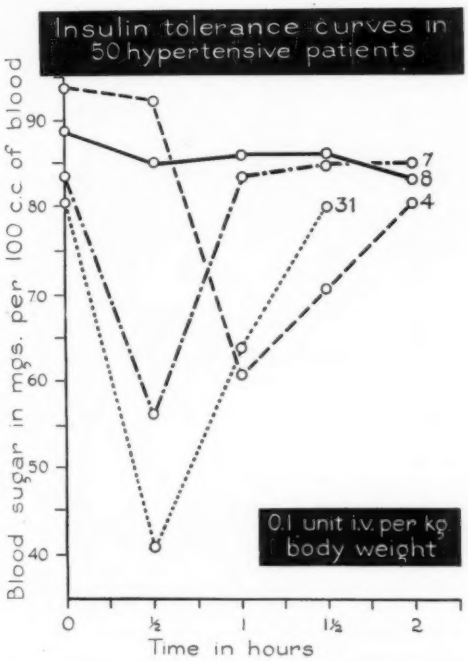

FIGURE 4. The insulin resistance of the hypertensive patient. Note that out of 50 patients 31 showed a normal response; 4 patients showed a slightly diminished response, but 8 showed a complete and 7 a partial resistance to the intravenous dose of 0.1 of a unit of insulin per kilogram of body weight.

Their reaction to splanchnicectomy is at first completely negative. The blood pressure does not fall, nor does their response to insulin change. Later examinations, however, indicate that after three months the blood pressure begins to fall and they become insulin-sensitive.

There has been sound experimental evidence cited in a previous paper[11] that epinephrine stimulates the adrenal cortex through the mediation of the pituitary gland. Thorn and his co-workers[13] described the fall in circulating eosinophils, when adrenocorticotrophic hormone (ACTH) was administered and indicated this test to be a sensitive index of adrenocortical reserve. Later Thorn substituted epinephrine for the pituitary hormone which is hard to purify and difficult to obtain.[14] In a group of hypertensives our tests indicate a diminished cortical reserve which improves after splanchnicectomy (Figure 5); this would fit into the concept of increased cortico-adrenal stress in some hypertensives, who notoriously complain

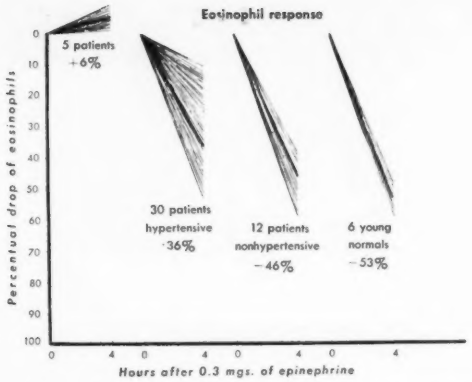

FIGURE 5. Eosinophil counts are made by a special technic before and three hours after the intravenous injection of 0.3 mg. of epinephrine in 200 cc. of normal salt solution. More recently, the epinephrine has been given subcutaneously and undiluted. A paradox response has been observed in allergic individuals (first column). Hypertensives usually showed a diminished cortico-adrenal reserve, the maximum response being obtained by young normals.

of fatigue as one of the first symptoms. Following splanchnicectomy the cortico-adrenal reserve, if originally low, may increase (Table 6).

The failure of splanchnicectomy in patients affected with cortico-adrenal hyperfunction can be remedied by removing an adenoma or, in case of a simple hypertrophy, by resecting part of the gland. This partial adrenalectomy has been practiced by some surgeons in the past, but solely with the idea of decreasing secretion of epinephrine. It is still in the experimental stage, and it should be recalled with what trepidation Theodor Kocher did his first thyroidectomies. Attention should be called to the fact that adrenal denervation, which is effected by dorsolumbar sympathectomy and splanchnic nerve section, shows histologic and physiologic changes in the adrenal cortex, and that delayed favorable response to splanchnicectomy may well be due to this effect.

TABLE 6

EPINEPHRINE EOSINOPENIA FOLLOWING SPLANCHNICECTOMY

PATIENT	PREOPERATIVE	BETWEEN STAGES	FINAL	REMARKS
S. B.	10	13, 31, 34	55	Cort. Ext.
L. M.	48	28, 38	47	" "
B. M.	27	54	53	
T. L.	50		50	
R. S.		10	44	
B. F.	41	33	48	
E. M.	53	29	62.2	
Th. K.	29		54	

SUMMARY

The causes of failure in the surgical treatment of hypertension have been discussed from four viewpoints. The evaluation of the *psychic factor* may call for a postponement or refusal of the operation. Combined with psychotherapy, surgery is still possible in selected cases. The *extent of sympathetic denervation* has to be determined in each individual case and a minimal and a maximal procedure were described.

Fifteen operations were done, the results of which would suggest that the removal of the upper two lumbar ganglia was more important than the extension of dorsal sympathectomy above the ninth dorsal ganglion. The *irreversible renal factor* was studied with the help of a water tolerance test, and it was pointed out that hypertensive renal damage was much more fixed than cardiac or retinal damage. For this reason, irreversible renal ischemia often vitiates the results of sympathectomy. The *adrenal factor,* particularly cortico-adrenal hyperfunction, has also been studied with the help of the insulin tolerance and the epinephrine-eosinopenia. A certain group of patients whose response to splanchnicectomy was either delayed or absent, was thus recognized. With more restricted indications the mortality, morbidity and percentage of recurrence can be gradually decreased.

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CLINICAL STUDY

Treatment of Amebiasis

RESULTS WITH DIODOQUIN AND CARBARSONE

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(This paper and the two which follow report on studies being conducted by the Veterans Administration on parasitic infestation in veterans.)

In a previous study it was found that amebiasis was a frequent finding in veterans with various types of complaints, chiefly referable to the gastrointestinal tract.[1] At the present writing, we have the records of approximately 1,000 cases of amebiasis in our files, accumulated since the start of this study in 1946. This large group of known cases plus the even larger group of yet undiscovered cases certainly presents a reservoir for the spread of the infection to the civilian population.

The incidence figures reported by numerous competent observers indicate that amebiasis is widespread throughout the United States, and that certain groups of veterans returning from highly endemic areas will increase this already large reservoir of infection.[2]

Markell, Mullinger and Schneider found 5.55 per cent of 1,153 military personnel infected and a 27.18 per cent incidence in 103 civilian internees from the Philippines.[3] The Tropical Disease Control and Laboratories Branches of the Office of the Surgeon General reported a 10 per cent incidence in 1,273 soldiers confined to United States service as against a 16.3 per cent incidence in 2,727 with overseas service.[4] Knight reported 11.8 per cent incidence among 296 dispensary patients in Chicago.[5] Many other reports in the literature cite incidences ranging from 5 to 20 per cent in the United States. These will not be cited in detail here.[2,6] Craig's estimate of at least a 10 per cent incidence for the United States is probably as close to the truth as is possible.[2]

In our own experience we have not been able to check the veterans' families for evidences of spread. However, we know of several dozen infected families which were diagnosed by the Detroit Health Department Laboratory and our own.[7] In many instances entire families have been found infected. Several have been almost impossible to cure probably because of rebound infections from one member to another. This might be labelled "ping-pong" amebiasis, to borrow the term often applied to syphilitic reinfections.

The disease is undoubtedly widespread and one more example may be cited here. A local physician with an extensive practice discovered 16 cases in 37 problem patients whom he referred to a competent laboratory for stool examinations. None had been previously suspected as having amebiasis and all had had extensive examinations of all types without a definite diagnosis. There was one death in this group following surgical drainage of an intraperitoneal pelvic abscess per rectum. An initial diagnosis of cancer of the colon had been made in this patient.[8]

DIAGNOSIS

Two factors are pre-eminent in the diagnosis of amebiasis: (1) awareness of the disease, and (2) competent laboratory diagnosis.

In our previous paper, we reported our own laboratory technics. Experience and training are the most important factors involved, as was previously stated. Unfortunately there is no universal standard laboratory method or methods for the diagnosis of amebiasis. Perhaps this is not really as important as it seems, but it does render the comparison of incidence figures difficult, if not impossible, between laboratories using different diagnostic methods.

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An attempt has been made since our last report to evolve an ideal simplified diagnostic method. The procedures of Mackie[9] and our own have been combined, simplified and streamlined as much as possible in an attempt to obtain maximum diagnostic accuracy with minimum of effort. The PVA-fixative technic of Brooke and Goldman[10] has been found very useful and time saving. Our present laboratory method is as follows:

1. Following magnesium sulfate the first *three* stools are to be collected from each individual and delivered to the laboratory.

2. *No. 1 specimen* (first stool passed after salts) is to have routine examination consisting of direct smears with saline and iodine and zinc sulfate concentration. A culture will be done on this specimen and read after 24 hours (Cleveland-Collier medium). The 48-hour culture will be discontinued as routine unless subculturing is desired. *No. 2 and 3 specimens* are to be examined for trophozoites by direct smears (saline and iodine plus Quensel's stain). Iron-hematoxylin smears will be made for permanent record and diagnostic confirmation when *Endamoeba histolytica* is found or suspected on direct examination or in culture.

3. Attention is drawn again to the following steps in routine procedure: (a) the importance of looking macroscopically for minute flecks of mucus in *all* specimens, and examining several such flecks immediately; (b) the importance of immediate examination on delivery of specimen for typical motility. When this is not possible specimens must be placed in the incubator, and examined as soon as possible.

PVA-FIXATIVE TECHNIC IN THE DIAGNOSIS OF AMEBIASIS

Trophozoites of intestinal amebae disintegrate rapidly and consequently it is often difficult to get laboratory confirmation of suspected cases of amebic dysentery or amebiasis. The polyvinyl alcohol (PVA) fixative technic furnished a means of preserving these fragile organisms for subsequent examination. Fecal specimens or other materials suspected of containing trophozoites can be mixed with PVA-fixative—a mixture of fixative and water-soluble resin. Films subsequently prepared from such preserved material can be stained by various hematoxylin procedures and trophozoites demonstrated if originally present.

PREPARATION OF THE PVA-FIXATIVE

REAGENTS

1. Modified Schaudinn's solution
   - Glacial acetic acid ..... 5.0 cc.
   - Glycerol ..... 1.5 cc.
   - Schaudinn's solution ..... 93.5 cc.
   - (2 parts saturated aqueous solution of mercuric chloride and 1 part 95 per cent ethyl alcohol)
2. Polyvinyl alcohol (PVA) powder* ..... 5 gm.

Add the powder to the solution at room temperature and then heat to about 75° C. After cooling, the solution should be clear and free of lumps. PVA-fixative remains satisfactory for several months and can be used either at room temperature or heated to 50° C.

PRESERVATION OF SPECIMENS WITH PVA-FIXATIVE

It is important to fix specimens immediately after passage from the patient, before the organisms lose their characteristic morphology.

On microscope slides—A drop of dysenteric stool or other material is placed on a microscope slide and mixed with 3 drops of PVA-fixative. The mixture is then smeared over approximately two-thirds of the glass surface and allowed to dry thoroughly (preferably overnight at 37° C.). Dried smears remain satisfactory for staining for many months.

In vials—A quantity of specimen is thoroughly mixed in a vial containing 3 or more parts of PVA-fixative. Smears for staining can be prepared immediately or months later by spreading a drop or two of the mixture over the surface of a microscopic slide. It is important not to have the smears too thick and to allow them to dry thoroughly.

STAINING OF PVA SMEARS

PVA smears are permeable to all commonly employed staining reagents. Such smears are therefore handled by the same method as smears fixed in the conventional manner with Schaudinn's fixative.

A variety of hematoxylin technics can be used but the long Heidenhain iron-hematoxylin procedure gives best results. The Tompkins-Miller technic (Am. J. Clin. Path. 17:755, 1947) is a more rapid method that has given uniformly good results and in most instances is satisfactory for diagnosis.

*Produced by E. I. Dupont de Nemours and Co., Electrochemical Department, Wilmington 98, Delaware, and designated as Elvanol 90-25.

Regardless of the staining procedure to be used, dried films are placed first in 70 per cent alcohol containing iodine for 10 to 20 minutes in order to remove mercuric chloride crystals. It is preferable to protect the stained film with a mounted coverslip; however, the uncovered films can be satisfactorily examined with the oil immersion objective.

A distinct advantage of PVA-fixative is that it makes possible successful staining of organisms occurring in fluid specimens. The solution serves as an adhesive as well as a preservative and prevents loss of organisms during the staining procedure.

A TWO-VIAL METHOD OF SHIPPING SPECIMENS

PVA-fixative was developed primarily to preserve trophozoites of intestinal amebae. It is not entirely applicable to the diagnosis of protozoan cysts and helminth eggs. Therefore, in order to make possible the recovery of all stages and types of organisms occurring in stools a two-vial method for shipping specimens is recommended. A portion of *freshly* passed feces is introduced into one empty vial and into one containing PVA-fixative. The sample is thoroughly mixed with the preservative. Both vials should be sent to the diagnostic laboratory with appropriate identification. The same system can be employed by public health organizations as well as by hospitals and clinics where there are frequent delays in transporting specimens to the laboratory for examination.*

This proposed ideal method was evolved by us after discussions with Kessel,[11] Cope,[12] and Callender.[13] If the diagnosis of *E. histolytica alone* is desired, probably the combination of culture with the PVA-fixative stain technic would yield the highest accuracy with the least effort.

THERAPY

It is our purpose here to report the results of a continued follow-up on a large group of these patients after a single course of therapy with DIODOQUIN and CARBARSONE.

There have been many drugs proposed for therapy of amebiasis in the past, and when so many drugs are listed the suspicion always arises as to just how effective any of them really are. Emetine was not used, because of its toxicity, in ambulatory patients.[2,14,21]

Probably the two most widely used drugs in the United States are: (1) Diodoquin (Searle) (5, 7-diiodo-8-hydroxyquinoline), and (2) Carbarsone (Lilly) (p-carbamidophenyl arsenic acid).

We, therefore, used both these drugs in treatment in an endeavor to determine just how efficient they really are on long term study. The dosage of diodoquin was 0.63 gm. three times daily for 20 days following the methods of D'Antoni[15] and Hummel.[16] Carbarsone was given 0.25 gm. twice daily for 10 days following Anderson and Reed[17] after completion of the diodoquin course.

The only toxic effects noted after administration of diodoquin were frequent mild diarrhea and pruritus ani. Following treatment with carbarsone one patient reported a mild skin rash which quickly cleared following cessation of the drug. The pruritus ani may be quite persistent and distressing. Carbarsone should not be given in the presence of liver disease.

CARBARSONE

Craig[2] believes that carbarsone will produce a cure in 85 to 95 per cent of patients after one course. Anderson and Reed[17] reported 90 per cent cure after one course of carbarsone. David, Johnson and Stanley[18] reported cures in 41 of 42 cases with carbarsone in one course.

DIODOQUIN

Richards reported 100 per cent cure after 21 days of treatment with diodoquin.[19] Karl and Sloan reported 96.0 per cent cure with the same drug.[20] Davis and Ritchie reported a 97 per cent cure rate with one course. D'Antoni[15] reported 81 of 84 cases cured. In 1948, D'Antoni began to have a few doubts and we quote him:[21]

> I began to use diodoquin in 1937 and up to about 13 months ago I was certain that it was the answer to our therapeutic problem. Since then, however, while this drug is still curing a large portion of patients, it is also failing with a large number, and the response in those who are eventually cured is extremely slow. I am continuing to prescribe it in preference to any other drug, because it can be used without toxic effects over a long period of time—as is now necessary, and it is at least as efficient as any other agent now commercially available.
>
> It is extremely unfortunate that the idea ever became widespread that emetine is a suitable agent

*From BROOKE, M. M., and GOLDMAN, MORRIS.[10]

for routine use. My experience has been that the supposed safety dose of 12 gr. is not safe at all.

THE last paragraph may be contrasted with Albright and Gordon's opinion that all infected cases should receive emetine.[14] We feel that emetine should be reserved only for complicated cases confined to bed in a hospital.

In our opinion, the crux of the matter as regards curability rests on the length of the follow-up studies. We have rechecked our cases every two months for one year whenever possible and then twice yearly for three years.

Amebiasis is a treacherous disease which may lie dormant for many months or years with little if any inconvenience to the person.[2]

On November 1, 1949, the files of 497 veterans were tabulated in an attempt to ascertain how many of these individuals were still negative for *E. histolytica* after one course of therapy. These veterans had had from 1 to 6 stool examinations after the therapy as outlined. It was obviously not possible to force anyone to return to the clinic for stool examinations but sufficient data were available to make a valid analysis (Table 1).

As can be seen from the table, there were 66 failures in 497 cases after one course of therapy with diodoquin and carbarsone. The group percentage of failure was 13.2 per cent. The percentage gradually became less as more examinations were made but there still occurred positive stools even after 5 successive negatives. It is very discouraging to discover a relapse after one or more years of negativity and presumed cure. In this respect, we have seen 5 veterans who were treated in service with emetine, carbarsone, and diodoquin between 1943 and 1945 and who were again positive when first seen by us as long as five years later.

TABLE 1

RESULTS OF TREATMENT WITH DIODOQUIN AND CARBARSONE

NUMBER OF TIMES EXAMINED	CASES	FAILURES	
		Number	*Per Cent*
1	188	41	8.2
2	127	13	2.6
3	92	6	1.2
4	47	1	0.2
5	27	2	0.4
6	16	3	0.6
TOTALS	497	66	13.2

The failures may be extremely resistant to treatment with any drug. Some of our failures are still failures after treatment with every amebacidal drug mentioned in the literature. We have come to feel that "cure" is the wrong word to use in relation to amebiasis. Perhaps it would be better to use the terms "arrested" or "apparent cure" somewhat in the same fashion as with syphilis or tuberculosis. Newer drugs to come may alter this somewhat pessimistic prognosis. Our data are now sufficient on aureomycin, CHLOROMYCETIN, and MILIBIS for preliminary reports which are now in preparation and will be published in the near future.

SUMMARY

1. Diodoquin and carbarsone are relatively efficient and nontoxic drugs for the treatment of amebiasis.

2. Long term follow-up is essential to proper control of amebiasis.

3. A certain percentage of cases may be very resistant to treatment.

4. Amebiasis is becoming increasingly prevalent in civilian contacts of veterans.

5. A standard ideal laboratory diagnostic method is proposed.

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Case Report

Treatment of Amebiasis

RESULTS WITH AUREOMYCIN

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SINCE the advent of antibiotics, they have been used in almost every disease of infectious origin. At first they were administered effectively in diseases of bacterial origin, then in those due to viruses and rickettsial bodies, and now we find them effective in certain protozoan diseases. Because aureomycin has been used in a relatively small number of cases of amebic dysentery and because the previous reports have shown it to be an effective nontoxic amebacidal agent, it was considered advisable to report the following case in detail.

This patient had had chronic gingivitis since 1942 which failed to respond to penicillin and local therapy and when he was first seen he also had an acute upper respiratory infection of three days' duration. *Endamoeba histolytica* were first found in his stools in December, 1948, and he was treated with emetine and DIODOQUIN, which were only of temporary therapeutic value.

CASE REPORT

F. W. B., a 30-year-old white married male, entered the Veterans Administration Regional Office on April 21, 1950, complaining of soreness across the upper abdomen, low abdominal cramps, diarrhea, and nausea and vomiting for the preceding two weeks. He had been having five to six loose watery stools daily. There was no blood or mucus in the stools. He stated that for the last three days he had had a common cold manifested by watering of the right eye, nasal congestion, coryza and a cough productive of whitish sputum.

A review of the patient's medical record revealed that he was in good health until he was inducted into the service on February 24, 1941. In March, 1941, he developed hepatitis following a yellow fever inoculation and was hospitalized for approximately six weeks and then recovered. The patient remained well until 1942. Up to this time he had attained a maximum weight of 165 pounds.

About June, 1942, he began to have abdominal complaints consisting of pain and soreness across the upper abdomen, low abdominal cramps and four to five loose, mushy, watery stools daily. There was no blood or mucus in the stools. He also had occasional nausea and vomiting. The patient was hospitalized and given symptomatic treatment to which he responded and was then discharged back to duty. However, he had a recurrence of his symptoms, and finally in November, 1942, he was admitted to Barnes General Hospital with a diagnosis of possible acute appendicitis.

While in Barnes General Hospital, it was noted that the patient had a chronic gingivitis. He stated that the condition was manifested by redness and soreness of the gums and bleeding, especially when he brushed his teeth. Under symptomatic treatment his symptoms cleared up. Upon examination he was found to have an enlarged spleen and was studied relative to the splenomegaly. No etiologic factor for this was found. The patient, however, was feeling quite well at this time and was finally discharged back to duty. At the time of admission to Barnes General Hospital his weight was approximately 142 pounds. From November, 1942, until approximately August, 1943, the patient had occasional attacks of abdominal cramps and diarrhea and occasional nausea and vomiting.

In August, 1943, the patient was sent to the European theater of operations and about this time he had a particularly severe attack of abdominal cramps and diarrhea and was hospitalized. He was treated symptomatically with fluids and paregoric and returned to duty. His weight at this time was about 140 pounds.

From September, 1943, to June, 1945, the patient continued to have intermittent attacks of abdominal cramps and four to five loose, mushy stools daily,

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accompanied by occasional nausea and vomiting approximately two or three times a month, each attack lasting approximately two to three days. The abdominal cramps were also accompanied by aching, pain and stiffness in the wrists and knees. During this time he stated that on one occasion, in 1944, he had blood in his stools. Throughout this period he was treated symptomatically by his flight surgeon with bismuth and paregoric. Finally, in June, 1945, upon the advice of his flight surgeon, the patient entered the hospital to try to determine the exact etiology of his condition. His weight then was approximately 130 pounds. From June, 1945, until January, 1946, the patient was hospitalized in numerous Army hospitals. The exact etiology of his condition was never determined and his abdominal symptoms persisted.

After discharge from the service, the patient received no treatment and finally, in December, 1948, he entered the Veterans Administration Hospital in Oakland, California. His weight at that time was 118 pounds. While there, motile trophozoites of *E. histolytica* were found in the stool after a magnesium sulfate purge. On the basis of this finding it was assumed that the patient had had chronic amebiasis since 1942, but that the organisms had never been found prior to December, 1948.

The patient was placed on emetine and diodoquin therapy. Under this therapy his symptoms cleared up, appetite improved, and he noticed a sense of general well being. By the time of discharge, on January 31, 1949, he weighed 130 pounds, a gain of approximately 12 pounds. After discharge from the hospital, the patient progressed fairly well until May, 1949, when he again had a recurrence of abdominal cramps, diarrhea, and four to five loose, watery stools daily and loss of weight to 123 pounds. He was again given some diodoquin but this therapy did not help. From May, 1949, until April 19, 1950, when the patient was first seen by the authors, his attacks of cramps and diarrhea were occurring approximately once or twice a week and would last two to three days.

Physical examination revealed a thin, poorly nourished, white male who appeared chronically ill. The temperature was 98.6° F., pulse 72, respirations 14, blood pressure 120/80 and weight 118 pounds. The pertinent physical findings were redness of the conjunctivae of both eyes; the right eye showed a moderate swelling of the upper and lower lids and a watery discharge was present. The nasal mucous membrane was reddened and congested and a serous discharge was present. The gums were red and spongy, and he stated that they bled easily upon brushing. The pharynx was moderately hyperemic. The abdomen was flat. The liver and kidneys were not palpable. The spleen was palpable about two fingers below the left costal margin. It was tender on palpation. The edge was blunt and smooth. There was some soreness and tenderness extending across the entire upper abdomen. Rectal examination was negative. Proctoscopic examination was negative.

The total white blood cell count was 6,050. The differential count showed 73 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 3 per cent monocytes, 2 per cent eosinophils. The red blood cell count was 5,480,000. The hemoglobin was 14.5 gm. A smear for malaria was negative. The sedimentation rate was 1.2 mm. per hour. The hematocrit was 45.5 per cent. Urinalysis showed the color to be light amber, the reaction alkaline, the specific gravity 1.020. There was a trace af albumin. Test for sugar was negative. Microscopic examination of the urine showed an occasional white blood cell. The cephalin flocculation test was negative. The icterus index was 10 units. The serum bilirubin was 1.1 mg. per cent. The thymol turbidity test was 2 plus. The van den Bergh test was slightly positive. Three stool examinations for *E. histolytica* were negative. The Wassermann and Kahn reactions were negative. The agglutination test for typhoid "O" was 3 plus at a dilution of 1:80. Agglutination tests for typhoid "H," paratyphoid A, paratyphoid B, proteus OX 19 and brucella were negative. The heterophil antibody reaction was negative.

The electrocardiogram was normal. X-ray examinations of the sinuses and of the chest were negative. A barium enema was negative. A flat plate of the abdomen showed a large, soft tissue mass (apparently spleen) which contained several small discrete calcifications, in the left upper quadrant of the abdomen. The liver also appeared to be enlarged, particularly the right lobe, which extended downward to the level of the iliac crest. The abdomen was otherwise negative.

The patient was started on aureomycin therapy on April 23, 1950, 500 mg. three times a day and at bedtime. Two days after initiating this medication he began to notice absence of soreness over the upper abdomen. The number of stools was reduced from five to six loose, watery, mushy stools to two formed stools daily. His appetite improved markedly and he also noted that the tenderness and bleeding of his gums when brushing his teeth had disappeared. His upper respiratory infection was cured. At the end of one week the dose of aureomycin was reduced to 250 mg. three times a day for three more days and he thus received a total of 16.25 gm. of aureomycin over a 10-day period.

By May 3, 1950, or 10 days later, the patient had gained 10 pounds in weight and had an increased sense of well being and vitality. A dental checkup after one week of therapy showed a clearing of his chronic gingivitis. Another check, two weeks after therapy had been stopped, showed normal gums.

While taking the aureomycin the patient had some nausea, but no vomiting. He complained of a sensation of slight dizziness and "hot flashes." He also noted a "pins and needles" sensation in the fingers of both hands. On the second day of therapy, he noticed a sweet taste in his mouth, and a feeling of burning about the rectum. Approximately five days after therapy was started he noted small, white papular lesions on the dorsum of both hands between the web of the thumb and forefinger. These areas became erythematous as he continued to take the medication; they were pruritic and assumed the size of approximately 4 cm. in diameter. With the discontinuance of aureomycin, all these apparent effects disappeared, the last of which was the skin lesions for which PYRIBENZAMINE ointment was prescribed locally and provided symptomatic relief.

Ninety days later the patient felt well and there had been no recurrence of the previously described symp-

toms. Hughes[4] considered his cases as "cured" if five warm liquid stools were negative for amebae after saline purgation two weeks after the patient received his last dose of aureomycin. Nevertheless, in all the references quoted the authors recognized the need for longer periods of observation before a "cure" could be considered permanent.

COMMENT

McVay, Laird and Sprunt[1] noted a change in the gross character of the stools as well as a decrease in the bacterial count in patients treated with aureomycin. R. I. Hewitt, in a personal communication to McVay et al., stated that aureomycin in vitro had an amebacidal effect on *E. histolytica*. This was confirmed by McVay et al., by introducing aureomycin into cultures of *E. histolytica* in amounts varying from 0.2 to 3.2 mg. per cubic centimeter. At the end of 48 hours no amebae were found in any of the cultured tubes. All the control tubes were heavily positive for *E. histolytica*. McVay et al. reported successful treatment in 14 cases. This initial report was soon followed by a single case reported by MacDonald,[2] the treatment of 8 patients by Most,[3] 7 successfully, and a report of treatment with aureomycin of 38 patients by Hughes,[4] 27 (71 per cent) being cured.*

Most summarized the present status of drugs used in treatment of amebiasis, enumerating the following:

1. EMETINE
2. IODO QUINOLINES
   - CHINIOFON
   - DIODOQUIN
3. METALS
   - CARBARSONE
   - THIOARSENITES
   - WIA
4. 4-AMINO QUINOLINES
   - CHLOROQUINE
5. ANTIBIOTICS
   - PARA-AMINOBENZOIC ACID
   - BACITRACIN
   - AUREOMYCIN

Terramycin might possibly be added to this list since the experimental studies in vitro and preliminary studies in a small number of patients have indicated that this drug may be effective in the treatment of amebiasis, according to the manufacturer. Despite this great armamentarium of drugs, many patients with *E. histolytica* infestations have undergone treatment with numerous courses of these drugs alone or in alternation with two or three of them. Hughes' series of cases reported ineffective treatment with carbarsone, diodoquin and VIOFORM, while a few failed to be cured by emetine and chiniofon.

Aureomycin was successful in 71 per cent of these cases. Emetine is of great value in the treatment of severe amebic colitis, amebic hepatitis or abscess, pulmonary, brain or skin involvement, as well as granuloma of the colon. Objection to its use is that it causes toxic reactions, notably upon the heart. There is also a high rate of relapse when it is used alone, and many chronic cases are highly resistant to the medication. The basis of the activity of diodoquin and chiniofon has been attributed to their iodine content. Rate of cure for these drugs is said to be 80 to 95 per cent; however, follow-up studies on large groups of patients are not available. Evaluation of the use of carbarsone, thioarsenites, and Wia (bismuth and arsenic in organic form) cannot be made at the present time because the total number of patients treated and adequately followed is still not sufficiently great. Chloroquine has been shown to have a moderate degree of amebacidal activity in colonic amebiasis. However, it has a high amebacidal activity in acute amebic hepatitis and abscess.

Of the antibiotics, para-aminobenzoic acid has been reported to have cured 4 of 9 patients (Dwork, quoted by Most). The frequency and size of each dose, as well as its relatively poor cure rate, preclude its use. Both bacitracin and aureomycin have been shown to be amebacidal in vitro. In view of the fact that these antibiotics also reduce the bacteria in the colon it may be that in so doing this they eliminate essential metabolites for the growth of *E. histolytica* and enhance its destruction.

The dosage of aureomycin has varied from 250 mg. four times a day for a total of 7 gm. over a period of four to seven days (Hughes), to a total of 24 gm. over a period of 19 days (MacDonald), or 500 mg. every six hours for five days and then 250 mg. every six hours for 14 days. In one case quoted by Hughes, a severe liver abscess which failed to respond to heavy and prolonged doses of aureomycin resolved promptly with emetine. Toxic effects from aureomycin noted by Hughes were heartburn,

*Since this report was submitted for publication, Gutch[6] has described the efficacy of aureomycin in the treatment of 20 patients with amebiasis and emphasized the lack of serious toxicity of this drug compared to other amebacidal preparations.

nausea, abdominal cramping, rectal and perianal burning. Our patient noted a sweet taste in the mouth, "hot flashes," "pins and needles" sensation in the fingers of both hands, a burning sensation about the rectum, as well as a toxic dermatitis of the hands.

In summary then, this case is of interest because under aureomycin therapy: (1) a case of amebic dysentery was cured symptomatically, providing additional confirmatory evidence of the efficacy of aureomycin in amebiasis; (2) a chronic gingivitis was cured; (3) an acute upper respiratory infection was cured; (4) there was a stimulation of appetite; (5) a toxic or allergic dermatitis developed following oral administration of aureomycin which, so far as is known to the authors, has not been reported elsewhere.*

*Since this article was written, Peck and Feldman[5] have described 3 cases of allergic skin eruptions following the oral administration of aureomycin.

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Treatment of Amebiasis

RESULTS WITH BISMUTH GLYCOLYLARSANILATE

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WITH THE TECHNICAL ASSISTANCE OF JOHN JEZA, R.T. AND RUTH ROSS, M.T.

VETERANS ADMINISTRATION, DETROIT

The incidence, symptomatology and treatment of amebiasis in World War II veterans have been discussed in previous publications.[1,2] The effectiveness of therapy with DIODOQUIN and CARBARSONE in consecutive courses was reported after long term observation.

Recently a new drug has been reported as effective against *Endamoeba histolytica* infection. This drug is bismuth glycolylarsanilate (MILIBIS).[3] It has been reported as having very low toxicity due to its low solubility in tissue fluids and poor absorption. It contains 15.01 per cent arsenic and 41.88 per cent bismuth. It should not be used in patients with known hypersensitivity to arsenic or by chronic alcoholics due to its solubility in alcohol. The recommended adult dose is 0.5 gm. three times daily for seven days. In the presence of diarrhea, larger doses may be needed. None of the cases reported in this paper had acute diarrhea, and they received only the above dosage.

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The supply of MILIBIS used in this study was provided by Winthrop-Stearns, Inc.

TOXICITY

McChesney and Hoppe[4] reported that milibis is almost completely nontoxic in rats when given orally. Absorption was studied in humans and rats. Both species excreted in the urine 2 to 4 per cent of the ingested arsenic at most. Human subjects excreted no detectable bismuth in the urine.

Brown[5] and his associates reported one case of arsenical encephalitis in a suspected alcoholic and a mild exfoliative dermatitis in another patient. These are the only reported instances of toxicity due to milibis. None of the cases in this series showed any toxic manifestations.

AMEBACIDAL EFFECTS IN VIVO AND IN VITRO

Dennis and his associates[6] reported that mili-

TABLE 1

RESULTS OF THERAPY AFTER ONE COURSE OF MILIBIS

NUMBER OF CASES	FAILURES	
	Number	*Per Cent*
36	4	11.1

Note: One of the failures has had 2 negative stool examinations after a second course of milibis.

TABLE 2

NUMBER OF STOOL EXAMINATIONS FOLLOWING TREATMENT (36 CASES)

EXAMINATIONS	NUMBER OF CASES
1	4*
2	3
3	9
4	15
5	3
6	2

*Failures; examinations averaged two months apart.

bis is amebacidal in vitro at dilutions of 1:30,000 to 1:35,000. They also demonstrated that it was very effective in hamsters. No toxic effects were noted in hamsters when the drug was administered for five days at 10 times the dose level required to cure all the test animals.

CLINICAL REPORTS

Milibis was first reported by Hauer[7] in 1943. He used it in German troops in Africa with both acute and chronic amebic infections and reported excellent results without toxic effects. Berberian[8] next noted in 1948 that 23 of 26 cases were cured after one course of the drug. The 3 failures were apparently cured after a second course. Dennis, Berberian and Hansen[6] stated that 31 of 34 cases were apparently cured by milibis in 1949. Brown[5] then reported 25 cases apparently cured after 12 weeks of observation. Berberian, Dennis and Pipkin in 1950 reported 62 (93 per cent) of 67 cases treated with milibis alone were cured after an average observation of 320 days.[12]

Following Berberian's report, it was decided to study the effectiveness of milibis in chronic amebiasis. A total of 36 cases was treated with the drug and the patients were followed for an extended period of time. The results, tabulated in Table 1, showed 4 failures in a total of 36 cases treated with one course of milibis as previously described. There were no toxic symptoms reported. In Table 2, it is noted that all 4 failures were found on the first recheck examination. This table records the number of recheck examinations for the whole group. The failure rate is 11.1 per cent. Table 3 shows a failure rate of 13.2 after consecutive courses of diodoquin and carbarsone. This took 30 days of treatment as compared to seven days for milibis. There were many complaints of mild diarrhea and pruritus ani after diodoquin and one mild dermatitis questionably due to carbarsone. It would appear that milibis is at least as efficient, better tolerated and more convenient for the patient than the consecutive courses of therapy with diodoquin and carbarsone previously used. None of the cases reported here had severe symptoms. All were ambulatory and were treated as outpatients.

TABLE 3

RESULTS AFTER CONSECUTIVE COURSES OF DIODOQUIN AND CARBARSONE

NUMBER OF CASES	FAILURES	
	Number	*Per Cent*
497	66	13.2

DIAGNOSTIC METHODS

No discussion of amebiasis can be complete without some mention of laboratory methods. These are adequately discussed in many standard textbooks on laboratory methods and are too seldom applied. Very few general diagnostic laboratories serving the practicing physician can do decent examinations of feces for ova and parasites. Laboratory technicians generally require far more training in this respect than they now receive. Physicians, too, should be far more aware of the widespread prevalence of amebiasis than they are at present.

A PROPOSED standard "ideal" diagnostic method was described in the previous paper.[2] The method is admittedly cumbersome and calls for trained personnel. In situations where purgation is not possible, immediate examination of several fresh daily formed stools by direct slides, cultures, concentrations and hematoxylin-stained slides may yield equivalent results. Sigmoidoscopy, with examination of aspirated material, is useful in selected cases but is not applicable for routine examination. In any case, competent stool examination will almost invariably reproduce the same findings.

DISCUSSION

What is important in the treatment of amebiasis is the actual cure rate, although this is extremely difficult to determine with any degree of accuracy. In this connection, it is felt that the true worth of any drug or combination of drugs can be appraised only after long term observation. It is the author's opinion that patients should be rechecked once annually for from three to five years after the first year of monthly or bimonthly stool examinations. This ideal is not too often attainable in practice. The question of reinfection will not be discussed since it can never be completely excluded, especially when familial infections exist.

It can be assumed that a varying proportion of parasites will be killed by any of the amebacidal drugs now available. Many of the survivors will be injured and their virulence reduced temporarily. Under such conditions, fecal examinations will usually yield negative results. However, the infection will again become evident after sufficient time has passed. For this reason, stool examinations should not be done more frequently than once monthly. Negative reports immediately after treatment are only useless and misleading. D'Antoni[10] has recently expressed similar opinions.

In reviewing the literature on treatment of amebiasis, one is impressed by the glowing reports of success with each new drug as it was introduced. Then, gradually, as the shortcomings of each became evident with the passage of time, the drug would either disappear or assume its true place in the therapeutic armamentarium if it had real value. Indeed, this has been true of many other diseases also. The usual pitfall has been failure to observe the patients over a long enough period of time. Many of the cases continue to have true morbidity, as well as serving as sources of infection, because they had been dismissed as cured by unwary physicians.

There is not available at this time any single drug which is the ideal anti-amebacide. All of the drugs in use are effective in a certain percentage of cases. A few cases will be extremely resistant to any therapy. Patience and persistence will almost invariably produce a good clinical result.

THE ideal drug will be without serious toxicity and will be effective against both intestinal and extra-intestinal infections. It is generally agreed that *E. histolytica* infection is always associated with tissue invasion of some degree, and that every case should be treated with drugs able to destroy the amebae in the tissues. The stumbling block has always been the fear of emetine toxicity, in spite of its widespread use for this purpose. Since the recent publication by Conan[11] of the effectiveness of chloroquine (ARALEN), we now have available for the first time combinations of drugs effective against *E. histolytica* anywhere in the body, and which are without significant toxicity. It is felt that every case of amebiasis in the future should have this combined type of treatment. Chloroquine alone will apparently cure about half of the intestinal cases also.

CONCLUSIONS

1. Milibis is apparently an efficient rapid treatment for intestinal (lumenal) amebiasis.
2. No toxic manifestations occurred in the group treated.
3. It is felt that amebiasis in the future should be treated with chloroquine (aralen) for systemic action, and with a drug such as milibis for lumenal action.
4. Long term observation is a necessity when treating amebiasis.
5. Awareness of the disease will result in the finding of many more cases of chronic amebiasis.

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Case Report

Aneurysm of the Left Ventricle

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Until the early years of the twentieth century cardiac aneurysms were considered extremely rare. This belief existed partly because no diagnosis was being made in many cases while in others the condition was being reported under the headings of angina or rupture of the heart instead of aneurysm.

In 1938, Parkinson, Bedford and Thomson[1] noted that among 457 cases of myocardial infarction reported by six different groups of investigators, the average incidence of cardiac aneurysm was slightly less than 9 per cent. This figure indicated clearly that aneurysms occurred more often than had been suspected. It should be noted, however, that this was the incidence among cases in which the outcome was fatal.

Although the foregoing has become fairly well recognized, the diagnosis of cardiac aneurysm during the patient's life is still comparatively rare. In 1914 only 3 cases had been reported, and in 1926 Pletnew[2] was able to find only 6 cases described in the literature. He referred to a seventh case and added another of his own. Even as recently as 1945 Fisher[3] emphasized the difficulties attendant on antemortem diagnosis. Credit for some of the diagnoses has been variously attributed to close observation of physical signs or to the utilization of roentgenologic and roentgenoscopic procedures. Of prime importance would appear to be an anticipation of aneurysmal changes in patients with an antecedent history of coronary occlusion, the expected frequency being approximately as already indicated. All these factors, with the exception of clinical signs, played a part in the diagnosis in the following case.

REPORT OF CASE

The patient, a traveling salesman, 53 years old, was first seen at the Mayo Clinic in 1936 and on several other occasions for advice regarding chronic eczematoid dermatitis. In June, 1949, substernal pain developed on several occasions while he was playing golf. This pain would come on while he was walking and disappear as soon as he stopped. He attributed the pain to "indigestion."

On July 29, 1949, the patient was awakened about 2 A.M. by substernal pain of such severity that he got up and paced the floor. Later in the day he called on a customer but terminated the interview because of the severity of the pain. He then drove about 250 miles to Cedar Rapids, Iowa, and was examined by Dr. R. M. Chapman who immediately hospitalized him and an anterior myocardial infarction was diagnosed. Adequate therapy was instituted, including administration of morphine sulfate, oxygen and anticoagulants. The patient remained in the hospital 71 days. On the forty-third day a roentgenogram was taken which showed enlargement and bulging of the left ventricle. A picture was not taken earlier because of the severity of the patient's illness. The sedimentation rate of erythrocytes remained high and was 79 mm. in one hour by the Westergren method shortly before his dismissal from the hospital.

Between October, 1949, and January, 1950, the patient's activities were moderately restricted, and he had no thoracic pain, shortness of breath or other complaints. The roentgenograms taken on September 9 (43 days after the myocardial infarction) and at the clinic on December 13, 1949, were similar (Figure 1). In December the patient's blood pressure was 140 mm. of mercury systolic and 86 diastolic.

On January 3, 1950, the patient complained of extreme fatigue. On January 4 he was seized by an excruciating substernal pain, which extended to the left arm. He died less than 15 minutes later.

Findings at necropsy—The heart showed left ventricular hypertrophy and weighed 685 gm. (estimated normal 333 gm.). In the left midventricular region there was a small degree of bulging over an area approximately 4 by 3 inches (about 10 by 8 cm.) in diameter. This represented the aneurysm seen in the roentgenogram. The extensive thinning and scarring of the myocardium in this region was reinforced by a closely adherent, laminated mural thrombus. Thinning of the myocardium and dense scarring extended to the apical and lower septal regions.

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FIGURE 1. The thorax showing the bulging out of the left border of the left ventricle due to the aneurysm.

Three centimeters from the origin of the left anterior descending coronary artery there was atherosclerosis, grade 3 (on a grading basis of 1 to 4) and narrowing, with a recent thrombus extending distally. Elsewhere the coronary vessels showed sclerosis of about grade 2.

The anatomic diagnosis was (1) hypertrophy of the heart (probably due to pre-existing hypertension); (2) coronary sclerosis of left anterior descending coronary artery with recent thrombosis; (3) old infarct of left ventricle with aneurysm and mural thrombosis; (4) focal calcification in the right adrenal gland; (5) hypertrophy of prostate and (6) lipogranuloma of prostate (one lesion).

COMMENT

This case presented several noteworthy features, some of which have been observed with comparative frequency while others have been encountered less often.

Among the first group we may list the age and sex of the patient, the cause of the aneurysm (myocardial infarction) and its anterior location.

As Crawford[4] pointed out, the presence of an aneurysm does not necessarily affect the clinical course. Of more importance is the condition of the remainder of the ventricle and its blood supply. In this instance it appears to have been adequate for the three symptom-free months intervening between the end of hospitalization and the second attack. Congestive failure or, as in this case, subsequent coronary occlusion is the common cause of death.[1,4] Rupture at the site of the aneurysm is an exceptional occurrence[3] and the densely adherent mural thrombus in many of the cases helps to explain why this is probably so.

Perhaps a more noteworthy feature of this case was the rapidity with which the aneurysm developed, apparently in somewhat less than six weeks. Among the 11 cases reported by Parkinson[1] in which there were antecedent infarcts the average interval was 17 months and the range was three months to seven years. Master[5] noted that most aneurysms developed after the infarcted area had become fibrotic and thin, and this is borne out in many of the cases reported in the literature. One of the shortest periods intervening between infarction and development of the aneurysm was reported by Shookhoff and Douglas;[6] in their case it was less than one week.

The treatment received by this patient appears to have been entirely adequate although there was

a serious lapse of time before the patient sought medical advice. It has been suggested by some observers that the incidence of aneurysm of the left ventricle has increased since patients with myocardial infarction have been treated with anticoagulants. This could have been a factor in our case, but a more important factor is probably the fact that this patient did not go to bed immediately after the onset of his pain. Instead he was up, walked about, drove his car 250 miles and did not go to bed until about 20 hours after the onset of pain. This is interesting in view of the frequency with which aneurysms were found by Dressler and Pfeiffer[7] to have been preceded by neglect of therapy; this neglect was due chiefly to the occurrence of coronary occlusions which had not been diagnosed at the time.

SUMMARY

In the case presented a cardiac aneurysm developed relatively soon after an acute anterior myocardial infarction. The condition was diagnosed during the patient's life. Some features of interest are compared with those in other reported cases.

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COMING MEETINGS AND POSTGRADUATE COURSES

United States Atomic Energy Commission, Washington 25, D. C.

Four fellowships in industrial medicine for the 1951-52 academic year. Awards are for one year's academic training at approved institutions of the fellows' own choosing. After completion of this training, fellows will be eligible to apply for a second year's in-plant training at one of the major installations of the AEC. Stipend for first year, $3600 plus tuition and laboratory fees; for second year, $5000. Open to citizens of the U. S. with an M.D. degree from an approved medical school and at least one year of internship. Applications should be submitted by March 1 to: AEC Fellowships in Industrial Medicine, Atomic Energy Project, School of Medicine and Dentistry, University of Rochester, Rochester, N. Y.

University of Oregon Medical School, Portland

Internal medicine, March 19-23. Course is under the auspices of the American College of Physicians. Application should be made to Mr. E. R. Loveland, Executive Secretary, American College of Physicians, 4200 Pine St., Philadelphia 4, Pa.
General surgery, March 12-16
Oregon Academy of Ophthalmology and Otolaryngology, spring postgraduate meeting, March 26-30
Electrocardiography, June 11-15

International Academy of Proctology, New York

Teaching seminar on proctologic subjects, in the form of a symposium and round table discussion, April 7. For registration or further information, write Dr. William Lieberman, International Academy of Proctology, 1819 Broadway, New York 23, N. Y.

National Gastroenterological Association, New York

Annual cash prize award contest for 1951—$100 and a Certificate of Merit for the best unpublished contribution on gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy. Contestants residing in the U. S. must be members of the A.M.A. Entries should be limited to 5000 words, typewritten in English, prepared in manuscript form, submitted in 5 copies accompanied by an entry letter and received not later than June 1, 1951. Address entries to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

The George Washington University School of Medicine, Washington, D. C.

Intensive postgraduate course in general medicine, including medicine, surgery, obstetrics and gynecology, psychiatry, anesthesiology and pediatrics, March 5-9

Wayne University College of Medicine, Detroit

The following continuation courses will be held from March 12 to June 9. For complete information, write the Office of Postgraduate Medical Education, 1512 St. Antoine St., Detroit 26, Michigan. Registration must be made before March 10
Pathology of neoplasms, Wednesdays
Pathology of the heart, Fridays
Advanced hematology, Mondays
Seminar in dermatology, Wednesdays
Conference on venereal diseases, Thursdays
Medical conference, Wednesdays
Gastroenterology, Saturdays
Medical seminar, Thursdays
Medical x-ray conference, Tuesdays
Surgery seminar, Mondays
Postgraduate course in early detection of cancer. May be taken for the entire year of three quarters or any one quarter may be selected

American College of Chest Physicians, Philadelphia

Fourth annual postgraduate course in diseases of the heart, at Hotel Warwick, Philadelphia, March 26-30. Applications should be sent to the American College of Chest Physicians, 500 N. Dearborn St., Chicago 10

American Trudeau Society, medical section of the National Tuberculosis Association

Three postgraduate courses in thoracic diseases in conjunction with the following schools:
Harvard Medical School, Tufts College Medical School and Boston University Medical School, Boston, the week of March 26
Marquette University School of Medicine, Milwaukee, the week of March 26
Albany Medical College, Albany, New York, lectures on 5 successive Thursdays beginning March 29

AT THE CLINIC

GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist, with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

Treatment of Bulbar Poliomyelitis

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BROWN

BAKER

It is well known that in bulbar poliomyelitis, the viral agent may produce pathologic alterations within any of the nuclei of the brain stem. Involvement of the upper cranial nerve nuclei, although resulting in disturbing symptoms, does not jeopardize the patient's life and requires very little treatment on the part of the physician. The only exception is the involvement of the motor part of the fifth cranial nerve, which when irritated may produce a severe trismus. The inability of the patient to open the mouth jeopardizes the patient's nutrition and may greatly interfere with adequate suctioning of the patient's secretions if the lower cranial nerves likewise become involved. The presence of such a trismus should be regarded by the physician as a medical emergency and tracheotomy should be considered in every case, since this is the only method of keeping the patient free of secretions and the airway open.

In most cases of bulbar poliomyelitis, the most severe and dramatic symptomatology arises from involvement of the ninth and tenth cranial nerve nuclei. Involvement of these nuclei produces difficulty in speaking and in swallowing. Because of the latter, there generally results an accumulation of secretions within the oropharynx often producing an obstruction of the airway and asphyxiation of the patient. This latter complication must be kept in mind in every patient with bulbar poliomyelitis and must be treated very diligently if one is to avoid severe complications or even a lethal outcome. Since it is possible in most cases to keep the airway open through various medical procedures, fatalities from this type of bulbar poliomyelitis can invariably be avoided. Specific procedures in handling such cases will be discussed later.

In approximately 30 per cent of the cases of bulbar poliomyelitis, the infection implicates the autonomic nuclei in the medulla, producing injury to the respiratory and the vasomotor centers and resulting in cardio-respiratory symptomatology.

*From the Division of Neurology, University of Minnesota Medical School, aided by a grant from the National Foundation for Infantile Paralysis.

Such symptoms may occur in the absence of specific cranial nerve involvement or may be associated with difficulty in deglutition. Any patient with bulbar poliomyelitis, even in the absence of severe cranial nerve involvement, who shows evidence of respiratory irregularities, or who develops rapid alterations in blood pressure or pulse rate, must be considered as a critical case of bulbar poliomyelitis with severe involvement of the autonomic centers and must be treated accordingly.

Before proceeding to the specific measures used in handling the various types of bulbar poliomyelitis, it might be well to outline briefly some of the general measures which should be considered in the treatment of all cases.

GENERAL MEASURES

Isolation—Although at best a relative state, isolation serves both to protect the attending personnel and more important it serves as a device which aids in *minimizing secondary infection of the patient* while in a state of lowered resistance. In view of our lack of knowledge regarding the transmission of the viral agent, isolation is best continued.

Fluid balance—The importance of measuring the fluid intake and output is well known. The daily intake is judged on the output which in addition to the urinary output must include the fluid removed from the lungs by suctioning. An intake between 2,500 and 3,000 cc. per day is adequate.

Feeding—Bulbar poliomyelitis implicates the nerves subserving deglutition. Feeding during the acute stages is accomplished by the intravenous route. Glucose and protein substitutes although insufficient in their caloric value except in large quantities are basic to the patient who cannot swallow. Where possible, a nasal tube should be introduced. The presence of a tracheotomy tube does not contraindicate the use of a nasal tube. An attempt should be made to provide the patient with at least 2,500 calories per day.

Excreta—Strict adherence to isolation is necessary in the disposal of the patient's excrement.

Catheterization—In many patients with bulbar poliomyelitis, catheterization is necessary during the first few days. The well known precautions concerning emptying and care of the catheter apply. Urinary tract infections may be minimized by the use of small amounts of sulfadiazine given orally or intravenously.

Vital signs—A running record of the pulse, temperature, respiratory rate and blood pressure is of help in evaluating the progression of the disease and the development of autonomic dysfunction.

Chemotherapy—Penicillin should be administered to all cases more as a prophylactic than as a specific viricidal agent. There is no indication for other antibiotics at present.

Medications—Sedatives are contraindicated. Atropine serves no useful purpose in the control of secretions because of the tendency to make secretions thicker, more tenacious and therefore predisposing to atelectasis.

Physiotherapy—Hot packs are in vogue at present and are more effective in the acute stages. Their effectiveness is partly physiologic and partly psychologic. Physiotherapy assumes increasing significance with chronicity of the disease.

Vitamins—High vitamin intake, especially vitamins B_1 and C, is indicated particularly in those cases whose food intake is hindered. Intramuscular and intravenous preparations are available and practical to use.

Observation of progression—Of considerably greater importance than the previously mentioned measures is the observation of progression of the disease. It is in the early recognition of the spread of the disease process into the brain stem and vital centers that prompt measures for the prevention of anoxia incident to obstruction of the airway can be instituted. Failure to appreciate an ascending infection from the spinal cord to the brain stem may result in a fatal outcome. To be cognizant of the clinical symptomatology resulting from progression requires trained personnel. Of tremendous help is the mandatory presence of nursing personnel over a 24-hour period. The presence of trained nurses, however, does not relieve the physician of his responsibilities in checking the patient frequently during the day and night. In addition to the cooperation of the nursing profession the services and cooperation of the otolaryngologist are mandatory.

ILLUSTRATIVE CASES

The following cases are selected to demonstrate the various procedures as applied in the handling of the patient with bulbar poliomyelitis.

***Case 1**—Mild nonprogressive bulbar poliomyelitis:* A 16-year-old white male first became ill with a slight fever, stiffness of the back muscles and a temperature of 104° F. On admission to the hospital the patient spoke with a slight nasal twang, showed marked difficulty in deglutition, and definite pooling of secretions in the back of the throat. The patient was able to swallow only slight sips of water. There was no paralysis of the limbs. Spinal fluid showed 50 cells, mostly mononuclears. The patient was immediately placed in a Trendelenburg position and constant pharyngeal suction was instituted for the secretions. The patient was fed intravenously and the vital signs were watched carefully. During the next five days the patient's temperature gradually dropped to normal. There was no progression of the bulbar symptomatology. By the seventh day the patient was able to swallow with greater ease and subsequently showed a rapid and uneventful recovery.

Discussion—This case illustrates a relatively pure

FIGURE 1. Method of intratracheal suction through three-way tube connected with tracheotomy tube. The large corrugated tubes conveying oxygen and carbon dioxide are connected with the three-way attachment.

bulbar poliomyelitis which apparently remitted during the early part of the course. It should be emphasized that as long as the airway can be kept open with drainage and suction no further radical procedures should be instituted.

Case 2—*Severe progressive bulbar poliomyelitis without intercostal or diaphragmatic involvement:* A 19-year-old female was first seen four days after the onset of a severe headache and backache. On the day prior to admission the patient had developed severe nausea with vomiting and a fever of 102° F. A spinal puncture by her local physician showed 145 white cells, mostly mononuclears. On the day of admission, the patient had developed a weakness in the right upper extremity, a slight nasal tone to her voice and some difficulty in swallowing, having regurgitated fluids through her nose.

On admission the patient had a paralysis of the right side of her face and moderate pooling of secretions in her throat. Her voice was hoarse and had a slight nasal intonation. Her pulse was 115, her temperature was 103° F., her blood pressure was within normal limits, the respirations were 30. Because of the pooling of secretions in the pharynx, the foot of the bed was elevated for postural drainage, and 24-hour nursing care with constant suction of the secretions with a Müller suction was immediately instituted. Careful records were kept of her pulse, temperature, respirations and blood pressure. The respirations, blood pressure and temperature remained fairly constant during the next three or four days, suggesting that there was no involvement of the autonomic centers. However, 24 hours after admission the patient showed increasing speech difficulty and it became impossible to keep her airway cleared by suction.

Because it was impossible to keep the airway clear by postural drainage and suction, tracheotomy was performed on the second day after admission to the hospital. Suction was then maintained through the tracheotomy tube and the patient was given additional oxygen through a three-way attachment to the tracheotomy tube (Figure 1). During this entire period the patient was given intramuscular penicillin, 100,000 units every four hours and was routinely turned in bed every hour in order to prevent the onset of pulmonary complications.

During the first three days in the hospital the patient was fed intravenously. On the fourth day as the temperature began to drop, a nasal tube was inserted and the patient was fed small feedings at frequent intervals in order to prevent aspiration of food. The patient's temperature gradually dropped. By the tenth day in the hospital her swallowing had begun to return so that she could take sips of water. On the fourteenth day the tracheotomy tube was closed. The patient continued to improve, even though some of the bulbar muscles remained weak for months after discharge.

Discussion—This case represents an almost pure case of involvement of the cranial nerve nuclei with disturbance of deglutition and talking. This type of involvement comprises about 60 to 70 per cent of all cases of bulbar poliomyelitis. The physician's attention must be directed particularly to the prevention of an obstruction of the airway and asphyxiation of the patient. In all such cases an attempt should first be made to keep the airway open by postural drainage and by suction. If this is impossible, then one must be prepared to perform a tracheotomy before the patient becomes moribund or develops cyanosis. Chemotherapy and proper turning of the patient should also be included to minimize pulmonary complications.

One must *never place a patient with bulbar poliomyelitis alone, in a respirator.* The presence of a partially obstructed airway in a patient in the respirator will invariably hasten pulmonary complications and will result in death from pulmonary edema. Only in the additional presence of paralysis of the peripheral muscles of respiration should a patient with bulbar poliomyelitis be placed in a respirator. This will be discussed in a later case.

***Case 3**—Bulbar poliomyelitis with involvement of the autonomic centers:* This patient was a 25-year-old white male. Three weeks before his admission to the hospital he developed a slight fever, pain in his back and stiffness in his neck. A spinal puncture performed by his local physician revealed 600 cells all of which were polymorphonuclear. Upon admission to the hospital the patient showed marked nuchal rigidity, a temperature of 102° F., a pulse of 100, respirations of 20 and a blood pressure of 120/80. There was no paralysis or weakness of the muscles.

During the next day the patient's condition continued to progress. He developed some weakness in the left lower extremity. On the second hospital day he showed a slight facial weakness, a nasal twang to his voice and a slight difficulty in swallowing solid foods. It was apparent at this time that he now had some involvement of the brain stem. The pulse, respiration and blood pressure were graphically recorded. During the third and fourth days in the hospital, the patient's pulse rate gradually increased to 160, and his respirations varied between 20 and 60 per minute. His blood pressure fluctuated greatly, at times being highly elevated and at other times being almost at shock levels. The patient, however, continued to swallow liquids without too much difficulty. It was apparent that this patient was now having a severe involvement of the autonomic centers and that because of the disturbed respiration and circulation he was suffering from inadequate oxygenation of the nervous system.

During the next 24 hours the patient became extremely apprehensive and confused and had some periods of cyanosis. These latter symptoms were present in spite of the fact that he showed good action of his diaphragm and some residual action in his intercostal muscles. A tracheotomy was performed and the patient was given additional oxygen through the tracheotomy tube. He was also continued on penicillin, and was turned constantly. His condition remained critical for a number of days. On the fourteenth day his temperature gradually dropped and he began to show considerable improvement.

Discussion—This case illustrates the methods followed in observing and handling a case of bulbar poliomyelitis in which there is an involvement of the autonomic centers. In cases with severe autonomic involvement it is frequently necessary to do a tracheotomy earlier than in patients with pure obstructive symptoms because of the desirability of having some means of increasing the oxygenation of the patient. If an oximeter is available and if one is able to determine if the oxygen saturation of the patient has not dropped in spite of the autonomic involvement then one can defer tracheotomy until such a time that this oxygen deficiency becomes apparent. It must be kept in mind, however, that patients with bulbar poliomyelitis who develop autonomic symptoms do not do well once they have developed a period of cyanosis. A tracheotomy done after the development of this complication generally is not of too much avail, since the hypoxia which has resulted not infrequently will damage cells already injured by the virus and result in irreversible changes from which the patient does not recover.

Patients with autonomic involvement are extremely sensitive to sedative drugs. Even after apparent recovery, a small dose of sedation may result in complete cessation of respirations and a lethal outcome in a patient who previously had been doing very well. Nutritional requirements of these patients are handled similarly to those of patients with pure defects in swallowing.

***Case 4**—Bulbar poliomyelitis associated with paralysis of the muscles of respiration:* A 35-year-old housewife was admitted to the hospital with a five-day history of headache, fever and weakness of both upper extremities. At the time of her admission, the patient showed a complete hyporeflexia with a marked paresis of the right upper extremity. The cranial nerves were intact; spinal fluid revealed 60 cells most of which were mononuclears. During the next 24 hours, the patient's course was rapidly progressive. She developed a complete paralysis of the intercostal muscles, weakness of the diaphragm and a nasal quality to her voice. It was apparent at this time that we were dealing with a bulbo-spinal poliomyelitis.

The patient was watched very carefully, because it was apparent that any further weakness of the diaphragm would require the use of a respirator. The additional complication of bulbar involvement made it necessary to watch the patient carefully for obstructive symptomatology. Within the next few hours the patient's diaphragm became completely paralyzed and she was immediately placed in the respirator, after which she became comfortable and her color improved. During the next 24 hours the patient's bulbar symptoms continued to progress. She developed increasing difficulty in swallowing in spite of constant suction. It soon became apparent that it would be impossible to keep the airway open without more radical procedures. A tracheotomy was therefore instituted. The patient was given intramuscular penicillin and even though in a respirator, was turned constantly to prevent the development of pulmonary complications.

Despite the suctioning and the tracheotomy, on the fifth day after admission the patient began to show signs of bronchial obstruction which could not be cleared by the most intensive suctioning. Bronchoscopy was performed through the tracheotomy tube and large mucous plugs were removed. The patient immediately improved. This procedure was repeated frequently during the next few days. Throughout the entire period that the patient was in the respirator, careful notice was made of her pulse, temperature and respiration. During the first few days she was fed in-

travenously, but as her temperature began to drop a nasal tube was inserted and feeding was continued through the nasal tube. After the third week, definite improvement was noted and the patient continued to improve although it was months before she was able to get along without her tracheotomy tube because of the excessive secretions and her inability to cough.

Discussion—This case demonstrates the extreme rapidity with which this disease may spread throughout the brain stem and spinal cord. It also demonstrates the need for intensive medical supervision to combat the patient's symptoms. Complications in bulbar poliomyelitis are always more frequent when the patient has an associated involvement of the muscles of respiration and requires the respirator. It might be pointed out that bronchoscopy is a relatively harmless procedure for a patient who already has a tracheotomy and should be instituted as frequently as is necessary to keep the airway open.

CONCLUSIONS

It might be re-emphasized that one of the most frequent complications in bulbar poliomyelitis is due to the involvement of the lower cranial nerves producing an obstruction of the airway. Such an obstruction of the airway can result from the following causes: (1) a pooling of secretions due to paretic throat muscles; (2) paralysis of the tongue; (3) obstruction of the airway due to reflex spasm of the laryngeal musculature; (4) obstructed airway due to an abductor paralysis of the vocal cords; (5) aspiration of vomitus. In addition to the above, patients may become hypoxic because of impaired circulation and respiration. Any of the complications listed will produce a definite sequence of symptoms and findings which should alert the physician to the presence of hypoxia and should make him check carefully for all those factors that may result in deficient oxygenation of the patient.

The symptoms of hypoxia in bulbar poliomyelitis in the early stages consist of restlessness and apprehension. As this condition progresses the patient develops an increasing pulse rate, blood pressure and respirations. Terminally, one will notice a marked dyspnea, cyanosis, some confusion passing into coma and shock. Prompt attention by the physician to these symptoms early in the illness may well prevent their increasing severity and may well save the life of the patient.

Rehabilitation of Poliomyelitis Patients

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DEAVER

So much has been written about poliomyelitis that physicians have become lost in a maze of details regarding the proper type of treatment. The result has been that many physicians, after making the diagnosis, send their patients to hospitals and place them under the care of specialists. This may be a wise procedure in the acute stage, especially if there is bulbar involvement, because of the facilities needed to care for breathing, swallowing and continuous or intermittent aspiration of mucus. Far too frequently, however, the family physician forgets about his patient and fails to see that adequate treatment is given.

If the child with muscle weakness is not given the proper type of physical therapy and braces he will usually develop deformities and become handicapped in meeting the physical demands of daily living. It is the family physician's responsibility to see that the proper treatment is given his patient in all the stages of the disease.

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THE ACUTE STAGE

When a patient with poliomyelitis is admitted to the hospital the usual method of treatment is as follows:

1. Maintenance of proper fluid and food intake and elimination of body wastes.

2. Proper lying position in bed. Prevention of prolonged back lying.

3. Relief from pain and tenderness. Drugs are

not effective and often dangerous. Moist heat in the form of hot packs tends to relax tense muscles and relieve pain.

4. Passive stretching is started as early as possible. The parts of the body should be moved gently, stopping before the patient has pain and before there is muscle spasm.

THE CONVALESCENT STAGE

When pain and tenderness are no longer present, the second step in the treatment program is to (1) evaluate the return of muscle strength, (2) start muscle re-education to the weak muscles, and (3) prevent deformities.

Muscle evaluation—There is a standard Muscle Test Form which can be obtained from the National Foundation for Infantile Paralysis. The Muscle Test Form lists the muscles and movements to be tested and the method of grading which is as follows:

KEY

MUSCLE EXAMINATION

Per Cent			
100	5 N	Normal	Complete range of motion against gravity with full resistance
75	4 G	Good*	Complete range of motion against gravity with some resistance
50	3 F	Fair*	Complete range of motion against gravity
25	2 P	Poor*	Complete range of motion with gravity eliminated
10	1 T	Trace	Evidence of slight contractility. No joint motion
0	0 0	Zero	No evidence of contractility
	S or SS	Spasm	Spasm or severe spasm
	C or CC	Contracture	Contracture or severe contracture

*Muscle spasm or contracture may limit range of motion. A question mark should be placed after the grading of a movement that is incomplete from this cause.

Muscle re-education—The object of muscle re-education is based on the hope that normal muscle strength will return. The success of this program depends upon the damage to the anterior gray horn cells, the skill of the therapist and the cooperation of the patient. Muscle re-education in small children is practically impossible because of the therapist's inability to obtain the child's cooperation.

Deformities—When there is an imbalance of muscles, deformities are likely to occur. It is necessary to maintain normal body alignment and this can best be done by light, removable casts or braces that are worn during the night and sometimes during the day.

How long should intensive muscle re-education be continued? The experience at Warm Springs indicates that the recovery of strength in muscles follows a fairly definite curve. At the end of the third month with proper treatment a muscle or muscle group will recover approximately 60 per cent of the total strength. During the second three months an additional 20 per cent returns for a total of 80 per cent. After this the recovery rate becomes increasingly slower and at the end of 18 months no further increase in individual muscle strength can be expected.

THE CHRONIC STAGE

After a period of approximately two years, we can expect no further return of muscle strength. If the patient has received adequate medical and physical treatment there are not likely to be any deformities. The treatment at this stage is to teach the patient, by means of braces, crutches, gadgets and the remaining muscle strength, to perform as many as possible of the activities necessary for daily living and working.

A study was made of 500 persons over 16 years of age with disabilities resulting from poliomyelitis who were tested in 99 activities under three categories: (1) ambulation and elevation, (2) self-care, and (3) the use of the hands.* It was found that there were 9 per cent who were classified as having no physical handicap, as they could perform all of these activities in a normal manner and with normal speed; 78 per cent had adequate compensation, and could perform all the activities, although not in a normal manner or with normal speed; and 13 per cent were unable to meet the physical demands of daily living and were practically homebound.

It is interesting to note that almost three times as high a percentage of persons in the miscellaneous group who had no hospital connections had inadequate compensation as compared with the hospital group, and 53 per cent of those in the miscellaneous series had serious disabilities compared with 39 per cent in the hospital series.

Of the 13 per cent who were homebound, at least 10 per cent of these could be taught to ambulate and care for their daily needs by proper physical rehabilitation.

CONCLUSIONS

The physician must assume the responsibility for his patient until he attains the maximum functional capacity to meet the demands of daily living and working. To attain this objective may require years of supervised treatment. The effect of growth, increasing weight, age and activity of the patient may

*This study was made at New York University-Bellevue Medical College by a grant from the Greater New York Chapter for Infantile Paralysis.

cause deformities even with the best of treatment. Simple surgical procedures may be indicated to prevent structural changes. Optimum results cannot be expected from orthopedic procedures until the patient reaches the period in which there is solid bone formation.

Treatment of Alopecia Areata

NELSON PAUL ANDERSON

LOS ANGELES

The successful treatment of alopecia areata has more to do with the art than the science of medicine. The host of entirely different therapeutic procedures, all of which have been used with considerable success, testifies to the truth of this statement. Many if not most of the patent medicine hair restorers, rejuvenators, mange cures, and the like owe their chief claim to fame to their success in causing the regrowth of hair in this capricious condition.

Nevertheless the condition can and should be treated, because of its psychogenic effect upon the patient. And furthermore success measured by the regrowth of hair will often crown one's efforts.

USE OF ULTRAVIOLET LIGHT

Among the office procedures which may be used is the application of ultraviolet light. This may be administered by means of the ordinary quartz light, the cold quartz light, or the carbon arc light. In instances where the loss of hair in patches is widespread such treatments may be given in gradually increasing doses to four areas of the scalp (e.g., the top, laterally and posteriorly). Care should be taken in such cases to protect the ears and skin adjacent to the scalp by means of a clean towel which covers the forehead, ears and posterior neck. It should be applied fairly tightly and held in place by a hemostat. The first or test dose should be one which produces a mild erythema. The dosage is gradually increased by 15 to 30 seconds at weekly intervals until a total time of four to five minutes for each region treated is reached.

If the area of alopecia areata is small and solitary, one may use either the air cooled or water cooled ultraviolet if this is available. With either of these pieces of ultraviolet equipment smaller time exposures must be used. However, such small areas may also be treated by any ultraviolet light apparatus by making a window or opening in a paper towel. The protection at all times of the patient's eyes as well as those of the operator is to be stressed. Such ultraviolet light treatments should be given once weekly for three to four months or longer before they are abandoned.

If ultraviolet light therapy is not available or has already been tried without success one may paint small limited areas with pure phenol which is neutralized within 10 to 12 seconds by ethyl alcohol.

HOME TREATMENT

For local use at home the patient may be given stimulating and antiparasitic preparations in ointment form and containing 3 to 5 per cent of sulfur, *or* 3 to 5 per cent ammoniated mercury to either of which preparations 1 to 2 per cent of salicylic acid or 1 to 2 per cent resorcin, or both, may be added. Actually it probably makes very little difference what is used locally as long as both the patient and the doctor believe in its efficacy and as long as the preparation is applied with moderate friction once or twice daily. For those who prefer a stimulating lotion the following may be applied once or twice daily:

Rx	Bichloride of mercury	0.12
	Resorcin	4.0
	Chloral hydrate	4.0
	Tincture cantharides	15.0
	Alcohol 70 per cent	
	Distilled water aa ad	240.0

Note: Mono-acetate of resorcin or EURESOL® should be used instead of resorcin in patients with blonde hair.

In the majority of cases of alopecia areata of mild to moderate grades of severity the above measures usually are followed by a regrowth of hair. The first signs of regrowth in the scalp are manifested by the appearance of a fine, white, downy hair which can be seen best by examination in a cross light. On the beard the first sign of regrowth is also the appearance of white hairs which usually

can be felt more easily than they can be seen.

However there are cases of persistent alopecia areata and others of extensive and widespread alopecia areata. The latter may progress to an alopecia totalis not only of the scalp but also of the entire body. In this group of cases additional therapeutic measures include the correction of errors of refraction, the removal of foci of infection, especially dental foci, the administration of thyroid extract if there is evidence of hypothyroidism, or other endocrine preparations if indicated. In general the results of endocrine therapy and of vitamin therapy have been disappointing.

All of the above procedures are predicated on a correct diagnosis of the condition because in certain somewhat similar disorders such therapy as given might be harmful, i.e., lupus erythematosus involving the scalp.

Management of the Menopause

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WERNER

This article is entitled "Management of the Menopause," but a more appropriate title would be "Management of Hypo-ovarianism." A better title for the physical, functional, and chemical changes that occur in the body of a woman at approximately ages 40 to 48 years would be "The Climacteric."

The word "menopause" literally means cessation of menstruation, and cessation of menstruation at this age is the result of failure of the ovaries to respond to stimulation by the gonadotropic hormones of the anterior pituitary. Because the ovaries do not respond to gonadotropic stimulation, no follicles or corpora lutea are developed, and consequently no estrogenic hormone or progesterone is secreted, and no stimulation and growth of the endometrium occur, from which menstruation could result. Therefore, there is no menstruation and menopause results.

The chief reason to speak of menopause per se as the climacteric is that the climacteric is only one of the times during the menacme when ovarian hypofunction or afunction can produce the signs and symptoms characteristic for hypo-ovarianism.

These symptoms occur within a short time following bilateral oophorectomy. They frequently occur following unilateral oophorectomy, salpingectomy, or hysterectomy, due to disturbance of the blood supply to the remaining ovary or ovaries.

It is well to remember that hypo-ovarianism may occur at any time during the menacme, due to hypopituitarism, hypothyroidism, certain adrenal conditions, and ovarian malfunction. It may result from pelvic infections or contiguous inflammations. Severe general infections, toxemias, or anemias may cause disturbance. Except following castration, the symptoms of hypo-ovarianism usually do not occur during the menacme until the woman reaches approximately the age of 25 years.

It is important to obtain an accurate menstrual history in a young woman when she complains of subjective symptoms. Frequently the doctor asks the patient if she menstruates regularly and the answer is "yes." She may menstruate regularly, but not as many days as she formerly did and it may be very scant. This is important evidence for a diagnosis of hypo-ovarianism.

Hypo-ovarianism may be primary or secondary. It is primary when the ovaries fail to respond to normal gonadotropic stimulation, and it is secondary when there is insufficient pituitary gonadotropic hormone to stimulate normal ovarian function. The author is inclined to believe that failure of the pituitary to secrete sufficient gonadotropic hormones occurs very much less often than does primary failure of the ovaries.

The information that the writer wishes to convey or inculcate, is to remember that the symptoms complained of by women at the so-called "meno-

pause" are not only pertinent to that period, but are characteristic for ovarian afunction or hypofunction at any time during the menacme.

The administration of estrogens is substitution therapy, and is not a cure for the climacteric. The symptoms result from the endocrine imbalance, which in turn disturbs the nervous systems—central and autonomic. Cessation of menstruation is not the beginning or the end of the climacteric. It is only visible evidence that the ovaries of the woman are not functioning sufficiently to produce menstruation. Many women have characteristic symptoms of the climacteric and hypo-ovarianism while they are still menstruating. The endocrine imbalance can begin before and last long after cessation of menstruation. The woman will not be free of her symptoms until she develops that endocrine equilibrium characteristic for the postmenopausal period. This can take from one to ten years.

Estrogen therapy is given to keep the woman, as nearly as possible, in normal endocrine equilibrium and free of symptoms until she develops her own glandular balance, and then she is through the climacteric or menopause, so to speak. The only criterion we have that a woman is through the climacteric is that the symptoms do not return after cessation of treatment.

Estrogens are natural and synthetic. Natural estrogens can be made synthetically, but they are so easily, cheaply, and abundantly obtainable from urine of pregnant women and mares that this is the chief source of supply.

Synthetic estrogens, of which stilbestrol is the best known, are also obtainable. Stilbestrol frequently causes quite a few disagreeable side effects, among which are nausea and vertigo. The author has never had any unpleasant reactions from the use of natural estrogens.

TREATMENT

All patients should have a thorough examination upon which to base a correct diagnosis. Besides having endocrine dysfunctions, they may also have one or more of the hundreds of other ailments to which mankind is heir. If complete relief is to be had by patients, then there must be treatment and care for all of their abnormal conditions.

It is well to remember that almost all these women are subjectively nervous and the administration of a mild sedative helps to ease the patient until the estrogens can become effective. A ¼ gr. tablet of phenobarbital before meals and bedtime is usually sufficient, and in this dosage it is harmless. Some women are so extremely nervous when they first consult the doctor that they should have full dosages of sedatives until they become more calm.

The author has found that 5,000 I.U. of natural estrogens given intramuscularly every other day is uniformly effective in relieving the symptoms.

If the patient is not of menopausal age, the estrogen injections should be discontinued about seven days before the expected time for menstruation to give the patient an opportunity to menstruate. Immediately after the menstrual period treatment should be resumed.

If one wishes to use oral preparations, there are many of these obtainable in tablet or capsule form; the dosage depends on the type of estrogen utilized and the amount of active ingredients therein. These oral preparations may contain natural, conjugated, or synthetic estrogens. One daily or every other day is the usual dosage.

Treatment should be conducted under the strict supervision of the doctor, and should continue for some time beyond freedom from symptoms. If symptoms return after cessation of treatment, then it must be reinstituted. No one can definitely state to any patient the duration of treatment.

At the climacteric, some women become extremely subjectively nervous, melancholic, apprehensive, and psychotic; this is spoken of as involutional melancholia, or climacteric psychosis. The great majority of these patients are receiving various types of shock therapy. If these women are isolated and are given full doses of sedatives and intramuscular injections of estrogens, 10,000 I.U., they will recover as rapidly as they do from shock and without prolonged aftereffects, such as impaired memory.

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Pediatrics

IN GENERAL PRACTICE

For general practitioners, in whose practice is included a major proportion of the medical management of infants and children, and for the specializing pediatrician as well, POSTGRADUATE MEDICINE *presents this special regular department devoted to brief discussions by recognized authorities on their preferred methods of the treatment and management of diseases and problems of infancy and childhood.*

Immunization Procedures in Infancy

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THREE factors have led to the simplification of immunization of infants against diphtheria, pertussis and tetanus: (1) the enhancement of antigenicity of toxoids and vaccines by adjuvants such as alum, aluminum hydroxide or aluminum phosphate; (2) the purification and concentration of toxoids, and (3) the employment of mixtures of both toxoids with *Hemophilus pertussis* vaccine.

Satisfactory immunization against diphtheria, tetanus and pertussis can be obtained with three injections of such triple mixtures. Precipitated or adsorbed toxoid vaccines result in superior immunity with respect to diphtheria and tetanus when compared to "fluid" (neither precipitated nor adsorbed) mixtures. Furthermore, satisfactory protection against pertussis can be obtained at an earlier age when such adjuvants are used. Lastly, systemic reactions are less frequent with these more slowly absorbed mixtures. Triple mixtures in the "fluid" state without adjuvants, on the other hand, enjoy one distinct advantage. With them immunization can be accomplished more rapidly.

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In the past, before toxoids were purified, the larger amounts of adjuvant required resulted in frequent instances of sterile abscess or cyst formation. These are rarely seen now in the author's experience. Their occurrence may be minimized by the use of products injected in dosage volumes not greater than 0.5 cc. and administered by the intramuscular route. Alternate gluteal muscles are used for the first two injections and either the lateral aspect of the thigh or the deltoid is used for the third injection. The product should not coat the outside of the 1-inch 25-gauge needle used.

When precipitated or adsorbed diphtheria and tetanus toxoids containing pertussis vaccine are employed for routine immunization, the three injections of 0.5 cc. each are given at intervals of not less than one month. Longer intervals, however, are permissible, and actually result in higher final diphtheria and tetanus antitoxin levels. Long intervals, however, delay the attainment of protection against pertussis, the disease against which protection is most needed in infancy. Furthermore, because well infants are usually seen at monthly intervals for feeding advice, monthly injections are most convenient. If, however, because of intercurrent illness, an injection has to be omitted (and should be omitted, for sick infants may have severe reactions to the foreign proteins), the course is then resumed at the next monthly visit. It is by no means necessary to begin the course of three injections all over again.

When rapid primary immunization against

pertussis and/or diphtheria is desired because of the presence of an epidemic of one of these diseases, then "plain," "fluid" (neither precipitated nor adsorbed) triple antigen should be employed. Three injections may be given at intervals of two to four weeks. The volume of each dose will depend on the product employed and the manufacturer's instructions should be followed. Products in which one injection dose is incorporated in a volume of 0.5 cc. are preferable in the author's opinion.

The total number of killed *H. pertussis* organisms injected during the course of primary immunization is important. When precipitated or adsorbed products are employed, a total dose of 40,000 million *H. pertussis* is sufficient for the great majority of infants. For infants under 6 months of age, Dr. Sauer recommends 60,000 million cells divided into four monthly injections.[1] In the author's experience, this is not necessary, though admittedly a slightly higher percentage of infants should be protected thereby.

When no adjuvant is present (fluid mixtures or fluid vaccine), the total number of *H. pertussis* should be larger. The dosage should be not less than 80,000 million.

COMBINED IMMUNIZATION

The age at which combined immunization may be started has been the subject of much study recently. Although there is little need to immunize the infant against tetanus until he begins to walk, he is capable of synthesizing tetanus antitoxin during the first three months of life.[2] Active immunization against pertussis is, of course, desirable as early as possible. Sako[3] and his co-workers demonstrated that protection against familial exposure could be obtained when a course of three monthly injections of precipitated vaccine was started in the second month of life. He employed a total dose of 40,000 million *H. pertussis*. His work has been confirmed.[4]

On the other hand, immunization against diphtheria has long been known to be difficult during the first few months of life. Transplacentally acquired diphtheria antitoxin tends to suppress the primary immune response. When, however, Ramon's observation[5] that antitoxin production was enhanced by the presence of killed bacteria was applied to this problem, the suppressive effect of passively acquired antitoxin was in a large measure neutralized. In one study protective levels of diphtheria antitoxin were produced in 77 per cent of infants injected in the first three months of life with adsorbed double toxoids containing *H. pertussis* vaccine.[2] In another study, 92 per cent Schick negativity was obtained in a large group of infants injected at 2 to 5 months of age with only two injections of alum-precipitated diphtheria toxoid containing *H. pertussis* vaccine.[6]

One may conclude then that combined immunization with precipitated or adsorbed triple antigens may be successfully performed under 6 months of age. But is it desirable to do so? The arguments for and against early combined immunization will be summarized.

Pro—1. Protection against pertussis can be obtained during the early months of life when the disease is most dangerous.

2. Protection against diphtheria can be obtained in communities in which a large percentage of women of childbearing age have lost their early, artificially acquired immunity. (In the author's community 47 per cent of mothers of newborn infants have been found to be Schick positive.)

3. Local and systemic reactions are no more common at 3, 4 and 5 months of age than at 6, 7 and 8 months of age.

4. Fright on the part of the infant and the engendered fear of the doctor are negligible when the early schedule is employed.

Con—The capacity of the infant's immune mechanism is greater in the second six months of life than in the first six months. When combined immunization is delayed until the child is 6 months old, a firmer, more durable immunity against pertussis and diphtheria can be obtained with the same dosage.

It is the author's opinion that the balance of the argument is in favor of beginning immunization in the third month of life. If this is done, however, the first recall ("stimulating" or "booster") injection should be given one year after completion of the course, that is at 15 to 18 months of age. On the other hand, when primary immunization is deferred until the second half year of life, the first recall injection need not be given until two years have elapsed, that is at about 3 years of age.

RECALL INJECTIONS

The dosage employed in the previously mentioned initial recall injections should be 0.5 cc. of the precipitated or adsorbed mixture.

Thereafter, routine recall injections are probably necessary only every three years. Progressively smaller doses may be safely employed. When the child reaches the age of 10 to 12 years reactions to the diphtheria toxoid component of the mixed antigen may become marked. At this age the author discontinues the use of the mixed antigens. Triennial injections of tetanus toxoid, however, should be continued.

The question arises whether exposure to diphtheria, tetanus or pertussis during childhood is an indication for an emergency "booster." Each exposure should be evaluated. Certainly a puncture

wound or more extensive trauma is an indication for a "wound booster" of tetanus toxoid. Here one dose of fluid tetanus toxoid (0.5 or 1.0 cc., depending on manufacturer's instructions) is preferable to one dose of adsorbed or precipitated toxoid. A more rapid rise of antitoxin will be obtained.[7] (In exceptional instances, such as massively contaminated compound fractures, or when the patient is in shock, tetanus antitoxin should be simultaneously administered in a different region.) Passive immunization gives immediate protection and does not interfere with the secondary immune response.[8]

Intimate exposure of an immunized child to pertussis may occasionally warrant an emergency booster of 10,000 million *H. pertussis*. However, if the youngster's most recent injection of combined antigen occurred within a year this can be safely omitted.

Intimate exposure to diphtheria is an indication for an emergency recall injection of diphtheria toxoid. Here, as with tetanus, the fluid product is to be preferred.

PRECAUTIONS TO BE OBSERVED IN ROUTINE IMMUNIZATION

Systemic reactions can be minimized by adhering to the following dicta. Only well babies and well children should be inoculated. The presence of any illness, however minor, should be a contraindication to any prophylactic inoculation. An unusually long interval between injections rarely if ever interferes with the final development of immunity. Secondly, children with known cerebral damage should not receive *H. pertussis* vaccine or diphtheria toxoid. Children with histories of febrile convulsions should be inoculated first with a fractional dose. Likewise in asthmatic children fractional doses are advisable. However, in infants with eczema this does not appear to be necessary.

When an infant is brought in for his second injection, it is of the greatest importance to question the parent in regard to any reaction to the first injection. Somnolence should be inquired about as well as fever. When these symptoms are described, the volume of the next injection should be decreased to 0.1 cc. Febrile reactions in well children can be decreased by the routine prescription of aspirin to be taken a few hours after the injection. Local reactions can be minimized by limiting the volume of the injection to 0.5 cc. and by giving it intramuscularly.

Recent reports from England and Australia, summarized by Leake,[10] have strongly suggested a relationship between injections of diphtheria toxoid and *H. pertussis* vaccine, singly or mixed, and over 50 cases of paralytic poliomyelitis. These instances occurred during large epidemics of this disease. Injections of penicillin and of typhoid-paratyphoid vaccine have also been implicated in five instances. The theory has been advanced that the trauma of subcutaneous and/or intramuscular injections produce a *locus minoris resistentiae* at the corresponding level of the cord in individuals already harboring the virus of poliomyelitis. Paralysis of the injected limb follows.

No reports of similar fearful nature have appeared in this country as far as the author is aware. However, the foreign reports should alert us to the possibilities. It would be wise during epidemics of poliomyelitis to postpone elective injections of all sorts, just as we postpone elective tonsillectomy.

SMALLPOX VACCINATION

Smallpox vaccination can be performed at any time during the first year of life. The writer customarily does this at 11 to 12 months of age. It is convenient to perform a Schick test and a Mantoux tuberculin test at the same visit. The patient returns in five to seven days, at which time the vaccination is observed and the skin tests are read.

We now know that it is of the greatest importance to store smallpox vaccine at a temperature below 32° F. at all times. Failure to do so not only decreases the likelihood of obtaining primary vaccinia in an individual not previously vaccinated but, and this is more important, it may invalidate an immediate reaction in previously vaccinated individuals. In such persons Benenson[9] has shown that heat-inactivated vaccine can produce reactions that are morphologically indistinguishable from the immediate, so called "immune," reaction produced by potent living vaccine. Areolovesicular reactions, reaching their maximum intensity (greatest skin area involved) within 72 hours, have been produced with inactivated vaccine in sensitized individuals. These early allergic responses on the part of the skin to inactivated vaccine are ineffective in restimulating both clinical and serologic immunity. On the other hand vaccinoid reactions, that is reactions reaching maximum intensity (greatest skin area involved) between the fourth and seventh day, are apparently produced only by living vaccine.

Numerous cases of smallpox occurred among British and American troops in the Orient during World War II. In many cases, the patients' medical histories revealed records of recent "immune" reactions. Furthermore, when fresh, continuously refrigerated vaccine was administered to occupying troops, numerous instances of vaccinoid reactions, and even of primary vaccinia, were obtained in individuals who had exhibited immediate "immune" reactions on the last previous insertion.

How then can we be sure that we are restimulating immunity when we revaccinate a child? Benenson's comment is quoted:

> "Until a more stable vaccine is developed, the instability of living vaccine will continue to re-

quire storage of the material at the lowest possible temperature at all times prior to use, together with scrupulous adherence to proper vaccinating technic"—

that is, the multiple pressure method.

"Interpretation of the reaction after vaccination must be based on recognition that the early forms of reaction are not an index of activity of the virus used. Any reaction, regardless of its form, which is regressing by the fourth day merely indicates sensitivity; it connotes immunity only if that lot of vaccine is producing a significant number of vaccinoid or vaccinia reactions in other persons at the time."

Too often the local pharmacist is not aware that smallpox vaccine should be kept in the freezing chamber of his refrigerator. The doctor should remind him—and the doctor should do likewise.

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Treatment of Infantile Eczema

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Infantile eczema, it should be realized, is a purely descriptive label, and has no special etiologic or pathogenetic significance. Included under this caption are several conditions which are morphologically similar but which differ as to prognosis and special points of therapy. These are: (1) atopic dermatitis, (2) seborrheic dermatitis, (3) contact dermatitis and (4) mycotic eczema. Of these, the atopic and seborrheic varieties are the most common. This article will not make a distinction between these two because we believe that they cannot be differentiated except by time alone.

There are many contributing factors in the development of infantile eczema, such as heredity, dry skin, external irritants, infection, acquired hypersensitivities to certain foods or inhalants, and possibly psychogenic factors.

The atopic and seborrheic varieties of infantile eczema are variable in their onset and appearance, usually first occurring when the child is a few weeks of age. In the early stages they are most often characterized by an erythematous, dry, scaly papular eruption on the scalp and cheeks, which can become vesiculated and crusted. In more severe cases, the extremities may be affected and in some cases the eruption becomes generalized. Pruritus is extremely common and may be severe enough to be distressing. Frequently excoriations become impetiginized. Complications include disruption of normal hair and nail growth, local or generalized lymphadenopathy (dermatopathic lymphadenitis)[1] and fever. The duration of the disease varies with the individual. Usually there is clearing of the skin in two or three years. Some cases continue on into childhood and adulthood, and some patients develop atopic dermatitis, asthma or hay fever later.

In the treatment of infantile eczema, one should consider each of the following: (1) topical therapy, (2) avoidance of irritants, (3) avoidance of allergens, (4) contraindications and (5) general measures not included in the aforementioned considerations.

TOPICAL THERAPY

Skillful local therapy is most important. Medication varies with the stage of the eruption. In dry, erythematous, scaly areas, good results can usually be obtained with tar distillates. Crude coal tar, 3 per cent, or naftalan, 10 per cent, in Lassar's paste is effective but stains. We recommend the following prescription given by Ross and Brown:[2]

	PER CENT
Crude tar	2.5
Titanium dioxide	7.5
METAPHEN	1.0
BUTESIN	1.0
Zinc oxide	7.5
HYDROSORB (Abbott) base q.s.	

Subacute vesiculated areas and acute weeping and crusted areas of eczema usually respond best to a combination of wet dressings and lubricating ointments. Aluminum subacetate solution (N.F., 8 per cent) diluted 1 to 32 parts of cool water is mildly astringent, antiseptic and antipruritic. For the compresses, several thicknesses of cheese cloth or soft, thin white cotton cloth are recommended. These should be applied well moistened to the affected areas three or four times daily for 15 to 20 minutes. These dressings can be used about the eyes without danger of irritation. If there is generalized involvement, it is wise to treat only a third of the body area at one time to avoid chilling. Colloid baths can be used to advantage both to soothe and to allay itching. After wet dressings, which tend to dry the skin, a soft lubricating ointment should be used. Vioform ointment or cream (Ciba, 3 per cent) is excellent. On very young infants a 1 per cent strength is preferable. Its chief drawback is that it stains.

AVOIDANCE OF IRRITANTS

Irritation to the skin should be avoided by allowing only clean cotton clothing or bedding to come in contact with the skin. The infant's immediate surroundings should be clean, well ventilated, and light. Soap and water are to be avoided on eczematous areas, and cleansing should be done with either mineral oil or olive oil, using soft cotton pledgets and a little pressure. The colloid baths can be used for this purpose as well. The careful use of wet dressings and ointments softens scales and crusts, and helps to clean the skin. Fingernails should be trimmed closely. When local therapy does not control the pruritus, and bandages or cotton stockings over the hands do not prevent the child from excoriating, it may be necessary to place the arms in splints, or tie the extremities to the sides of the crib.

AVOIDANCE OF ALLERGENS

Potential allergens are to be avoided if at all possible. No woolen toys should be handled. The removal of rugs and curtains reduces dust. An infant who is nursing satisfactorily should not be changed to bottle feeding. The average infant with eczema secures little benefit from haphazard changes from one type of feeding to another. It is our opinion that, in general, food sensitivity plays an insignificant role in the genesis of infantile eczema. In the younger infant, dietotherapy may be more important than in the older child. In cases of sensitivity to cow's milk, it may be necessary to use substitutes such as goat's milk or soy bean products. However, with regard to the general problem of foods exacerbating an infantile eczema, we should like to quote from Cooke:[3] Twenty-seven patients with dermatitis of infancy and early childhood were hospitalized for dietetic study.

> "All the patients were tested by passive transfer, and the serum of 17 gave typical immediate wheal reactions to one or several foods. In 13, the positive tests were verified in part (one or more) by direct skin test. It was our intent to prove or disprove the causal relationship of the allergen giving an immediate wheal to the dermatitis in each particular reacting case. Except for the 9 patients acutely sensitive to egg, peanut or honey, the foods giving positive skin tests could be eaten abundantly and continuously without any exudative skin reaction. Egg, peanut or honey was fed in whatever amounts were possible. If eaten and retained, urticaria appeared promptly—*never dermatitis*—and these patients could eat all other skin test-reacting foods in quantity and indefinitely without developing any dermatitis."

In our opinion, cutaneous tests for the purpose of determining food sensitivities are not reliable and, therefore, desensitization therapy based on such data is in error.

CONTRAINDICATIONS

The topical application of sulfonamides, penicillin and streptomycin is contraindicated because of the likelihood of sensitization. Aureomycin may be an exception to this. Boric acid should not be employed in wet dressings or ointment on extensive areas, as toxic effects from absorption have been observed. Vaccination against smallpox should not be attempted in the presence of a severe eczema except under emergency conditions. Roentgen ray therapy may be of some temporary benefit, but we

feel this is radical treatment, and ill-advised. Ultraviolet light therapy is of questionable value.

GENERAL MEASURES

Antihistaminics are of doubtful value. Barbiturates in small divided doses are of limited aid in reducing pruritus. One of the best is elixir of phenobarbital, which contains 15 mg. (¼ gr.) per fluidram. An infant of 6 months can take 8 to 15 mg. per dose.

An infant with eczema needs more than physical attention. He is in trouble, and frequently is in severe discomfort. Kindness, assurance and a place for quiet rest are important.

We recommend as a good review of this subject the following: Hill, L. W.: Eczema in infancy and childhood. New England J. Med. 242:286-290 (February); 327-331 (March) 1950.

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Treatment of Vitamin Deficiencies in Infants and Children

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In the following discussion on the treatment of vitamin deficiencies, it is presumed that a correct diagnosis has been made. At the present time, some confusion exists in labelling conditions as being due to deficiencies of vitamin A and those of the B group. It should not be supposed that all cases of night blindness and conjunctival thickening are due to a deficiency of vitamin A or that all cases of capillary invasion of the cornea are due to a lack of vitamin B. Many more cases of roughened skin and cracked lips are due to exposure to wind and weather than to vitamin deficiency, and sucking colored lollipops more frequently causes tongue discoloration than does niacin deficiency.

VITAMIN A DEFICIENCIES

Treatment consists in the administration of 25,000 to 50,000 units of vitamin A daily for three or four weeks.

VITAMIN B DEFICIENCIES

In the therapy of all diseases due to a lack of one of the B group of vitamins, the presence of a deficiency of one or more members of this group must be considered. The fact that a preparation contains thiamine, riboflavin and niacin does not mean that all the members of the B group are present; the mixture will contain what is stated on the label but no more. One must not expect to obtain more than the antipernicious-anemia effect from a highly purified liver extract prepared specifically for the treatment of pernicious anemia. It is only through the incorporation of crude liver extracts, extracts of yeast, etc., that all the members of the B group are obtainable.

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HEMORRHAGE DUE TO DECREASE IN PROTHROMBIN

If through failure to administer a prophylactic dose of vitamin K to the mother at least four hours before delivery, or to the infant soon after birth, hemorrhagic disease of the newborn develops, treatment consists of the administration intramuscularly or intravenously of 5 mg. of one of the water-soluble K-like substances. Only very occasionally is a second dose necessary. Blood transfusion should not be resorted to as a therapeutic measure against the bleeding of hemorrhagic disease of the newborn because of the danger of increasing hemorrhage in some vital area before a normal clotting power has been established.

In hemorrhagic conditions brought about by decreased absorption of vitamin K from biliary stenosis or fistula, the administration of fat-soluble K by mouth, 1 to 2 mg. twice a day, must be accompanied by 2 gm. of bile salts with each dose. If hypoprothrombinemia should result through long continued administration of sulfonamide drugs or antibiotics, vitamin K may be administered by mouth in either the oil or water-soluble form, since here the fault is not in absorption but is due to deficient production in the intestinal tract

through decreased bacterial growth. Very occasionally, as the result of liver damage, inability to synthesize prothrombin occurs in spite of the presence of adequate amounts of vitamin K. In these cases bleeding may be treated by transfusions of whole blood or plasma.

RICKETS

The treatment of rickets consists of the administration of 2,000 to 3,000 I.U. of vitamin D daily for one month. Less chance of refusal or spitting up will result if this is administered in a daily dose of 15 drops of percomorphum oil or in a water-miscible form, than if one attempts to give the necessary amounts of 1 teaspoonful of a "brand name" cod liver oil, three or four times daily. To prevent the possibility of development of tetany which may occur in the healing of rickets, 10 gr. calcium lactate may be given three times daily.

More disturbing to the physician than rickets caused by failure to administer vitamin D is the form which occurs in spite of correct prophylaxis, most commonly in rapidly growing infants of premature birth. In these cases, although the dose of vitamin D is increased to the curative level and beyond, the craniotabes advances and slight deformity of the legs develops. Due to the premature birth the infant lacks the reserve stores of bone salts normally laid down in the last two months of pregnancy. Though the administration of vitamin D is producing optimum utilization of calcium and phosphorus, due to the small stomach capacity, the intake of minerals is not sufficient to allow proper calcification of the bones at the rate at which they are growing. The extra minerals needed may be provided by the incorporation of bone meal in the solid portion of the infant's feeding, or by the use of a skim milk formula where through lesser dilution more milk minerals are supplied in the same volume of feeding.

Very rarely a form of rickets develops in spite of administration of vitamin D and the intake of normal amounts of bone-forming minerals, which is not cured by normal curative doses of vitamin D; these cases may respond to daily doses of from 25,000 to 100,000 I.U. When doses of this magnitude are administered, excretion of calcium in the urine or its level in the blood should be followed. The administration of vitamin D in renal rickets is useless; here the treatment is that of the underlying condition.

TETANY

The possibility of sudden death, probably due to tetany of the heart muscle, in untreated cases of manifest tetany should always be borne in mind. The disease is an emergency to be treated immediately on diagnosis by the intravenous injection of a 10 cc. ampule of 10 per cent solution of calcium gluconate. This may be repeated at four- to eight-hour intervals over a period depending upon the persistence of the neuromuscular irritability and the recurrence of convulsions. In most cases at least 3 injections will be found necessary.

Calcium gluconate solutions should not be administered intramuscularly because of the danger of calcium deposits in the muscle, frequently going on to abscess formation. By mouth, calcium chloride, 15 gr. dissolved in 1 or 2 teaspoons of water should be given every four hours x 5 for two or three days after which the dose may be decreased to 10 gr. three times daily for three or four weeks. Should calcium chloride produce vomiting, a slightly larger dose of calcium lactate may be administered in its place. Antirachitic therapy as outlined under "rickets" should be started only after a week or ten days of calcium therapy, since its deposition in the bone may result in a further lowering of the blood calcium.

SCURVY

Due to the presence of substances other than ascorbic acid (vitamin C), clinical and animal observations have shown that orange juice is preferable to pure ascorbic acid in the treatment of scurvy. The daily therapeutic dose totalling 4 to 6 oz. may be administered in 2 or 3 divided doses diluted with an equal amount of water. No destruction of ascorbic acid occurs during a 12-hour storage of the extracted juice in a refrigerator, but it may be necessary to caution the mother against the addition of sodium bicarbonate. The attendant should be thoroughly aware that the orange juice is being administered as a medicine and not as a dietary supplement, which she may feel can be neglected for a day or so without untoward effect.

If, in spite of persistence, the orange juice is refused or vomiting or diarrhea occurs, it may be replaced by ascorbic acid, 100 mg. three times a day. The ascorbic acid tablets may be dissolved by mixing in a teaspoonful of water or formula which may be administered directly, or incorporated in a portion of the formula. The antiscorbutic should be administered at the therapeutic level for three or four weeks before being reduced to the prophylactic daily dose of, in infancy, 2 oz. of orange juice. Any accompanying anemia should be treated according to its severity by either transfusion of whole blood or oral administration of iron salts.

The curative effect of vitamin C in scurvy is so rapid that its administration may be used as a diagnostic test for the disease. Under adequate treatment, within 24 to 48 hours the patient is much less irritable and tender, within 48 to 72 hours the gums become less swollen and purple and are less apt to bleed, and after 8 to 12 days new bone, visible under the x-ray, is laid down beneath the stripped up periosteum.

Scientific Exhibit

Prosthetic and Sensory Aids Reference Exhibit

THE SEARCH THAT NEVER ENDS

MONROE H. LIPTON, EDUCATION SPECIALIST

DEPARTMENT OF MEDICINE AND SURGERY, VETERANS ADMINISTRATION

MAN has sought for centuries better aids to assist him in overcoming physical disabilities. This is a search that never ends—a quest for better artificial limbs, aids for the blind, hearing aids and other devices for the handicapped.

In the Veterans Administration Prosthetic and Sensory Aids Reference Exhibit, the development of prosthetic appliances is portrayed and the newest devices displayed to explain clearly and dramatically how, through the ages, there has been progress toward better appliances.

This exhibit is for the amputee, the blind, and the hard of hearing, to help them and their families to know what has been done and is being done by research to assist them. It is for the research worker and engineer who can view and study the thousands of items in the associated Reference Exhibit and the Library and try to improve them. The surgeon and the medical profession in general will find in the exhibit a complete display of prosthetic aids and orthopedic appliances, demonstrating quality of workmanship, methods of fabrication, and functional design.

The exhibit is open to all individuals and all groups interested in the field of prosthetics and sensory aids, and is located at the Veterans Administration New York Regional Office, 252 Seventh Avenue, New York 1, New York. Visiting hours are from 9:00 A.M. to 4:30 P.M.

The maintenance of the exhibit with contemporary artificial limbs, reflecting new developments, represents the Veterans Administration's desire to continue the search for appliances of better quality and function, and to assist all the nation's disabled through education, information and research. The display will be kept up to date with changing exhibits, showing the progress being made not only in the Government's program of research in this field, but throughout the world.

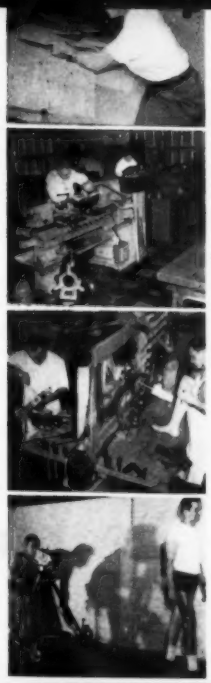
This exhibit represents the *Veterans Administration search that never ends.*

Veterans Administration personnel under whose direction this exhibit has been arranged include: Augustus Thorndike, M.D., Acting Director; Robert E. Stewart, D.D.S., Assistant Director for Operations, and Eugene F. Murphy, Ph.D., Assistant Director for Research, all of the Prosthetic and Sensory Aids Service, Department of Medicine and Surgery.

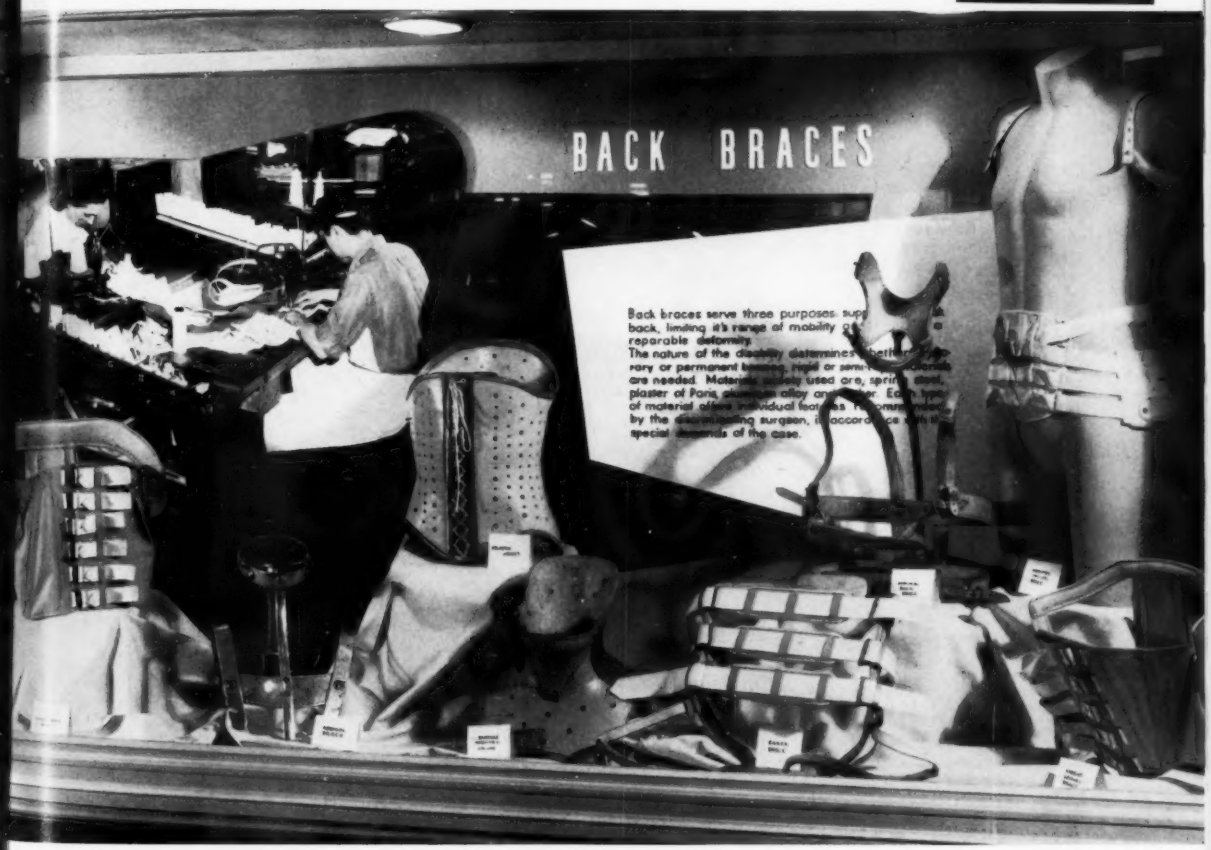
As part of the Veterans Administration Prosthetic and Sensory Aids Reference exhibit, the Research Section shows how the program, through contracts and the VA's own facilities, aims to initiate and conduct research and development with the ultimate objective of providing the best possible artificial limbs and sensory aids to disabled veterans through excellence in design, structure and performance.

View of the Prosthetic and Sensory Aids Reference Exhibit.

The Suction Socket display shows one of the recent research developments on above-the-knee limbs. This principle of suspension is based on the moderate suction created in the socket and the adherence of the skin to the walls of a well-fitted socket. There are no harnesses or belts on this type of limb.



Left and right, portions of the exhibit showing the work done by the Veterans Administration Prosthetic Testing and Development Laboratory in aiding the research program for disabled veterans.



Back braces commonly used and how they are made is the subject of this display.

A below-the-knee limb display exhibits the limbs made in this country and some of the problems encountered in fitting this type of limb.

A study of the various types of above-the-knee limbs reveals the different problems and some of the solutions possible in commercially available limbs.

Part of the Aids-for-the-Blind exhibit which shows the wide range of electronic and mechanical devices furnished blind veterans by the Veterans Administration to assist them in overcoming the physical disability of blindness.

A view of the artificial arms, hands and hooks exhibit shows the marked advances made during the past several years. A new type of hook (Army Prosthetics Research Laboratory) recently approved by the Advisory Committee on Artificial Limbs is the latest device.

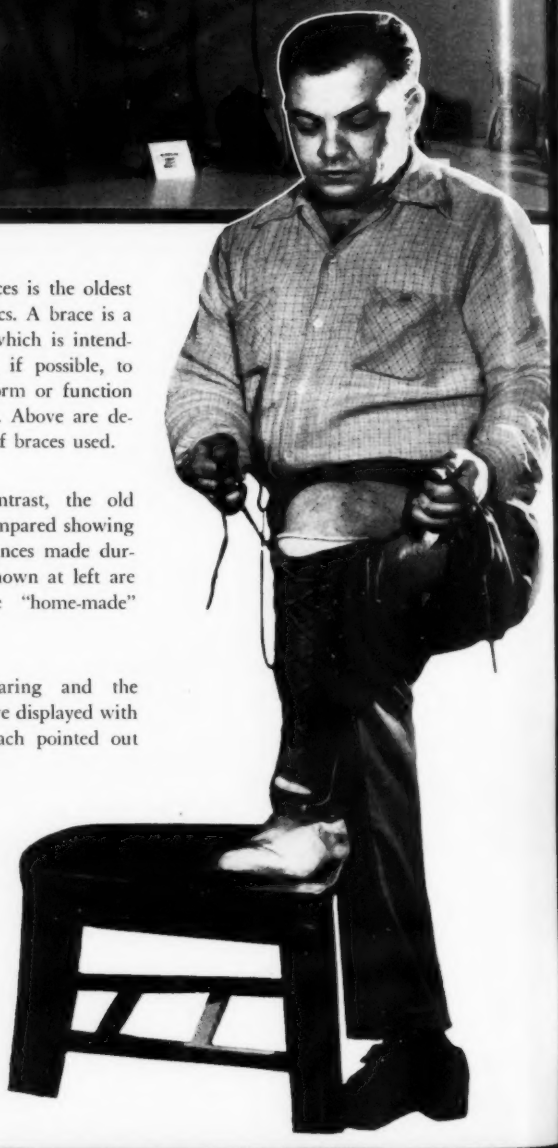
BRACES

The making of braces is the oldest branch of orthopedics. A brace is a mechanical device which is intended to support and, if possible, to correct defects of form or function of the human body.
Basic requirements for efficient brace making:
• Correct medical indication
• Scientific brace construction
• Good workmanship
• High-grade materials
• Careful fitting
• Intelligent use by patient

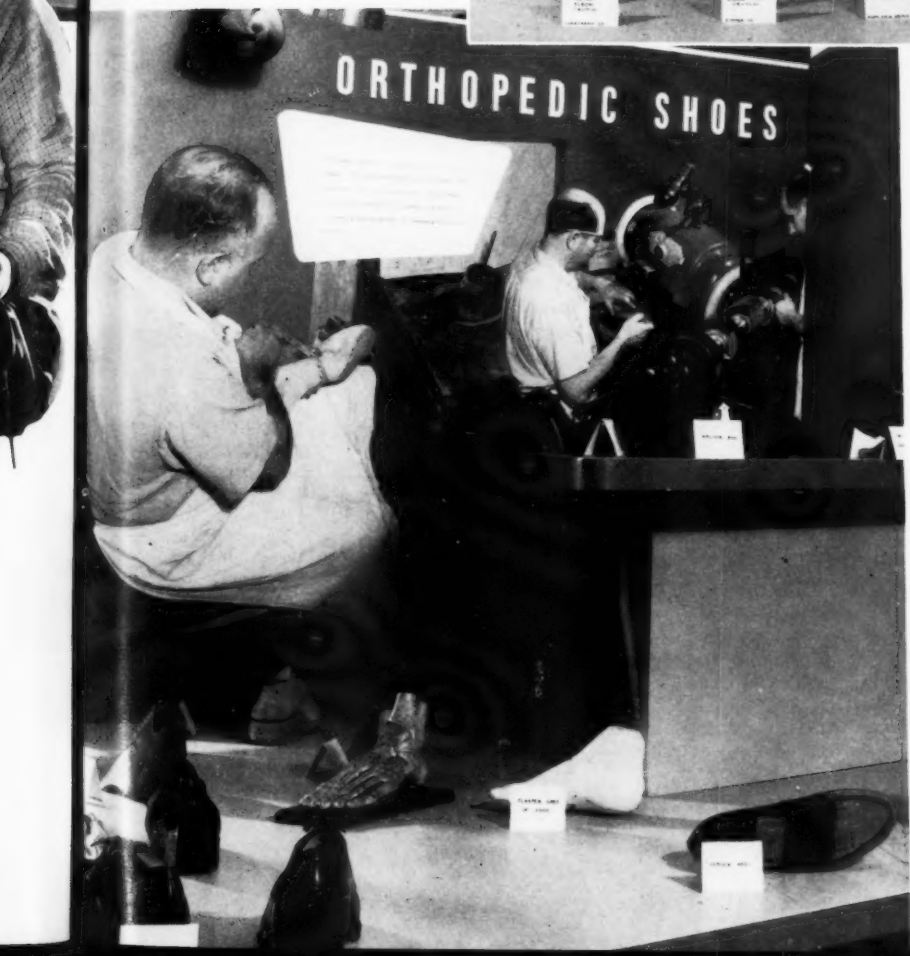
The making of braces is the oldest branch of orthopedics. A brace is a mechanical device which is intended to support and, if possible, to correct defects of form or function of the human body. Above are depicted many types of braces used.

Through vivid contrast, the old and the new are compared showing the significant advances made during recent years. Shown at left are examples of some "home-made" prostheses.

The knee end-bearing and the Syme's prostheses are displayed with characteristics of each pointed out (right).



Examples of crutches and canes show a diversity of appliances.



A complete exhibit of orthopedic shoes showing various types and how they are constructed is part of the display, only a portion of which is shown at left.

The exhibit above points out that certain materials are more readily adapted than others to the making of artificial limbs. Sound judgment, based on a careful consideration of the location of the amputation, the amputee's age and physical condition, as well as his economic and social status, should determine the proper materials.

Excerpt from the Hearing Aids display (left). Also included, but not shown here, are the modern devices available and the advances made in this electronic field.

The Plastic Eye and Cosmetic Restoration exhibit case (below) demonstrates the technics and examples of work. It shows the comparative appearance of individuals not wearing, and some wearing, these types of restorations.

PLASTIC ARTIFICIAL EYE
VA plastic artificial eye and restoration clinics in 15 regional offices and hospitals throughout the country produce plastic artificial eyes, facial and body prostheses and plastic ear hearing aid inserts for eligible veterans.
Each appliance is custom made for the individual patient at these various clinics.
A veteran is entitled to at least (2) two appliances and replacements as needed.

EDITORIALS

Postgraduate Medicine FOR THE CONTINUING EDUCATION OF THE PRACTICING PHYSICIAN

Editor-in-chief: CHARLES W. MAYO, M.D.
Contributing Editor and Editorial Writer: MORRIS FISHBEIN, M.D.
Assistant Editor: SYLVIA COVET

FEBRUARY 1951

HADACOL—APOTHEOSIS OF NOSTRUMS

When bigger and better nostrums are produced, the United States will no doubt produce them. When the Pure Food and Drugs Act was passed at the beginning of the century and more recently amended and when the Federal Trade Commission became effective and when the Post Office Department through its fraud orders clamped down on one antisocial medical promoter after another, the people in the United States should have been able to feel that they were at last well protected against nostrums and quackery. Then along came Hadacol to prove that the old medicine show with 1950 trimmings; the old nostrum exploited with extravagant and flamboyant claims for ordinary ingredients; the old radio technic for applying expensive box tops to the purchase of cheap prizes are just as potent a source of easy money as they ever were.

As recently as September 5, 1950, the Federal Trade Commission announced that the LeBlanc Corporation and its president, Dudley J. LeBlanc, had entered into a stipulation with the Commission wherein it agreed to discontinue certain advertising misrepresentations concerning the therapeutic properties of Hadacol. The Commission said in part: "They agree to stop representing that Hadacol has any therapeutic value other than such as results from the vitamin B_1, vitamin B_2, iron and niacin it supplies, and then only when clearly limited to cases resulting from a deficiency of one or more of these nutritional elements.

"The stipulation also calls for discontinuance of the representation that Hadacol has any dietary value except such as may result from providing vitamin B_1, vitamin B_2, iron and niacin, and one-third the minimum daily adult requirements of calcium and phosphorus."

According to the label, Hadacol is a mixture of some of the B complex vitamins and some minerals in 12 per cent alcohol. That means, children, that everything you can get from Hadacol you can get just as well—perhaps better—from any of the common, easily obtained B complex, plus minerals, capsules, except for the alcohol. But ah! that alcohol! In a dry state a good swig of Hadacol is about as potent as two scotches! You will think you feel better, children, even if you really are not.

Dudley J. LeBlanc is reputed by reports and magazines devoted to advertising to be selling about $2,000,000 worth of Hadacol a month. Dudley J. LeBlanc is a Louisiana State Senator. His road show included such

stars as Mickey Rooney and Connie Boswell. According to reports of those who have seen the caravan, it includes 100 van-type trucks, 30 Fords, Lincolns and Mercurys (donated by Ford Motor Company) for members of the personnel and members of two bands; two old-fashioned steam calliopes bring up the rear.

But LeBlanc is not depending simply on the patronage of the local yokels of the deep South who have a long record of easy acceptance of alcoholic nostrums. In addition to his medicine show, LeBlanc is reputedly spending $400,000 per month through the advertising agency known as Erwin, Wasey & Co., and has been using 700 daily and 4300 weekly newspapers and 502 radio stations with 4 to 16 spot announcements daily. This general advertising campaign is supplemented with special newspaper advertising in cities in which the show appears and with smaller schedules in country dailies and weeklies along the road. LeBlanc also buys a half hour TV time in each city in which the show appears and in which there is a local TV station. A report indicates that other members of the Louisiana State Senate accompanied him on a recent trip during which he distributed gold replicas of the 12,000,000th bottle of Hadacol to governors, mayors, editors and drug executives whom the caravan encountered en route.

Reports say that Hadacol began late in 1949 with 150,000 bottles per month and that the sales now approximate 2,000,000 bottles per month. Most recent in the exploitation of the LeBlanc Corporation, which is located at Lafayette, Louisiana, was a Christmas party, held December 23, in 1000 theaters, most of which were in the Southwest. In these 1000 theaters there were to be Hopalong Cassidy feature films with a Santa Claus in each theater, animated cartoons and personal appearances by local radio stars and, with all of this, gifts for all the children who attended. And the price of admission, children, in case you want to plan for next year's Christmas party, is just one box top from a package of Hadacol. *Tide* magazine says that the cost of the films and the theater rental alone amounted to $75,000.

When LeBlanc first launched Hadacol on the American scene, it was promoted as an "aid to nature in rebuilding pep, strength and energy of buoyant health when the system is deficient in the vitamins and minerals found in this tonic, provided no organic trouble or focal infection is present." However, the claims made for the product in the newspaper advertisements, which consist largely of testimonials, would indicate that the preparation had presumably cured the individuals pictured from such conditions as stomach ulcers, heart trouble, rheumatism, asthma, diabetes, high and low blood pressure, gallbladder disturbances and a variety of other ailments. A more recent advertisement cites a considerable number of people who seem to have been troubled principally with insomnia. One testimonial, from a 10-year-old boy who lives in Simms, La., testifies that he has been sick "for a good while," was nervous, could not sleep at night, did not want to study his school lessons. Then some of his friends told him about Hadacol. He has taken three bottles. Now he can sleep, is not so nervous, does not hate to get his school lessons and wants to tell his friends publicly about taking Hadacol.

Some of our more prominent investigators in research have suggested that glutamic acid has the power of influencing the I.Q. but, of course, Hadacol has not been submitted to the kind of controlled research that would involve the necessary psychologic tests!

An advertisement, published late in December, indicates that the campaign for the political advancement of Senator LeBlanc is coincidental with the campaign for the selling of Hadacol. From this advertisement there seems to be every indication that Senator LeBlanc has always championed the cause of the depressed, the poor and the underprivileged. He has worked for the veterans. Indeed this modest advertisement alleges, "His activities in public life in behalf of the working man are too numerous to mention here." Furthermore, "His tireless

study and effort resulted in today's wonderful Hadacol." What a study and what an effort it must have been to figure out a mixture of vitamin B complex and vitamins with 12 per cent alcohol! Really the senator should have been exhausted! But possibly he drinks Hadacol himself and in that way makes himself fit for his tireless efforts in behalf of Senator LeBlanc and Hadacol.

The Federal Trade Commission went on in its stipulation:

> "LeBlanc and the corporation further agree to cease and desist from exaggerating the frequency with which any disease, symptom or condition is due to a deficiency of vitamin B_1, vitamin B_2, iron or niacin.
>
> "Other representations to be discontinued under the provisions of the stipulation are that Hadacol assures good health, restores youthful feeling and appearance, does not contain drugs or influences health without the use of drugs."

Latest among the extraordinary demonstrations of showmanship by Senator LeBlanc is an advertisement which says that the LeBlanc Corporation wants a parrot which will say distinctly many times a day "Polly wants Hadacol." The owner of this highly intelligent parrot is going to be permitted to travel with the parrot and Senator LeBlanc throughout the nation in a limousine with the parrot's name engraved in gold on the door. The triumvirate will stop in only the best hotels. Furthermore, the parrot will visit large drugstores, perform at jobbers-salesmen meetings, conventions, etc., and may be present on radio and television.

What I want to see is an actual picture of the parrot drinking half a bottle of Hadacol and then saying in a clear distinct voice, "Polly wants Hadacol." This at least will prove the extent to which parrots are immune to the effects of alcohol.

MORRIS FISHBEIN

FEELING FOR THE FACTS

I HAVE just received a questionnaire from an agency called Fact Finders Associates which is conducting something called a foundation garment study. They want to know my opinion as to whether or not corsets, girdles and brassieres are important to women in the home, in business and in the factory. And not only that but also how important! They ask me, and no doubt they have asked many other physicians whether foundation garments contribute to good health, if they safeguard against fatigue and if they contribute to the efficiency of a person employed in business or in a factory. Then they ask how many women are employed in my organization and what per cent of these women habitually wear foundation garments during working hours. This last inquiry proposes a research on my part which my wife might regard as a little too intimate for a person of my position.

Just how do Fact Finders Associates propose that I determine with accuracy the per cent of my women employees who habitually wear foundation garments during working hours? Occasionally I have observed men of advancing years and decreasing mentality who seem to derive considerable stimulation from rather indiscriminate performance of the art of palpation, a simple method of physical diagnosis which rightfully used can lead to the accumulation of much interesting information. Yet Fact Finders Associates, Inc. do not even hint as to the technic that I should employ in determining the per cent of my women employees who habitually wear foundation garments during working hours and also the per cent who wear girdles, corsets and brassieres. What will Fact Finders Associates do with this information after I have sent it? I shudder to know! I do not think I shall undertake the necessary research to provide them with dependable answers.

As to the value of these physical supports from the point of view of health, I have no doubt that when properly constructed and when in the opinion of a physician who has made a study of his patient such equipment is recommended, it serves a useful purpose. During World War II the corset industry suffered because of controls placed on the use of rubber by the War Production Board. A distinguished scientific committee of the

Division of Medical Science of the National Research Council, of which I was a member, after extended consultation and discussion reached the conclusion that no great damage would be done to the public health if the supply of rubber for the construction of such devices should be limited during the war years. Hence such strange physical conditions as "stenographer's spread," "housewife's droop" and "flapper's flop" were permitted to progress until peace brought support to relaxing tissues. The available statistics regarding the course of the public health during the interval mentioned seemed to prove that no serious damage was done to the public health by the omission of these uplifting and supporting devices.

MORRIS FISHBEIN

SOVIET MEDICINE

Behind the Iron Curtain which surrounds the inner workings of the Soviet Government appear newspapers and periodicals which from time to time leak into the surrounding nations; thus information becomes available as to what goes on medically in Russia. Many Russian medical periodicals are regularly reviewed in the various sections of *Excerpta Medica.* These call attention to the rather strange adumbrations of the Russian mind in progress toward control of disease. Unfortunately such strange manifestations as the dicta on genetics and the long sleep treatment of peptic ulcer as well as the experiments of Bogomoletz tend to cast doubt on the quality of current Russian research.

Recently the New York *Times* cited some statements which appeared in an article by Professor M. Derzhavets in the *Literary Gazette* of Moscow concerning medical practice. Professor Derzhavets indicated that errors of diagnosis are frequent in Russian medical practice and that these errors are due to inadequate training and experience of physicians. He charged moreover that too many Soviet physicians were engaging in private practice to the neglect of their responsibility in the state medical system.

Another article in the same newspaper by one Dr. Olga Dzhigurda accused Soviet medical authorities of failing to provide sufficient quantities of medical instruments, apparatus and drugs. Moreover a newspaper known as Leningrad *Pravda* calls attention to many deficiencies in the organization of medical and hospital services.

These reports are not surprising. Revolution such as has occurred in Russia cannot cause a nation to step in a single movement from a situation in which the vast majority of its population are ignorant and underprivileged into circumstances enjoyed by the people of great democracies which have grown slowly but steadily for several hundreds of years. Regimentation has certain advantages in time of war when mankind in the mass is catapulted into conflict but history proves that progress comes more certainly when the fullest possible scope is given to individual initiative and private enterprise.

MORRIS FISHBEIN

CEREBRAL PALSY

Various estimates have been made as to the number of children in the United States with cerebral palsy. Most estimates agree that seven out of every 100,000 babies that are born have cerebral palsy. The total number of cases in the United States is said to be 350,000. Since the majority of cases of cerebral palsy arise from hemorrhage into the brain at the time of birth, what is learned relative to the care of such children bears some application to persons at the other end of the life span who suffer cerebral hemorrhage usually associated with high blood pressure and arteriosclerosis.

More than three-fourths of the children born with cerebral palsy have average or superior intelligence. Nevertheless the spastic movements which represent motor disabilities cause people in general to view these handicapped children askance and to

neglect the possibilities of education and development by which the majority of them could be developed into useful and in many instances exceptional citizens.

Almost the youngest among the foundations established in the United States to raise funds for research and rehabilitation in relationship to crippling disease is The United Cerebral Palsy Associations, Inc. which was organized August 12, 1949. Already this organization has served to educate great numbers of people as to the nature of the problem. Funds have been raised in considerable amount to be devoted to promotion of employment for such handicapped persons, and to provide scholarships and endowments for rehabilitation and education. The New York State Legislature appropriated $25,000 to train graduate therapists in the special problems of treating those with cerebral palsy in New York State and the Elks National Foundation established a similar fund to train such personnel elsewhere in our country. A competent board of directors including many leaders of industry, philanthropists and other prominent persons has been established and also a medical advisory committee under Dr. Winthrop M. Phelps as chairman and a research council under Dr. Sidney Farber as chairman.

Thus the United States proceeds in the democratic way to meet the problems inherent in the care of the handicapped and the disabled. What activity can be more in the democratic spirit than the banding together of persons of good will to aid those less fortunate and to promote the progress of medical science against the unsolved diseases!

MORRIS FISHBEIN

ELECTROPHRENIC RESPIRATION

THE ability to maintain adequate respiration is the difference between life and death. Under certain medical conditions artificial respiration becomes a matter of prime importance. When the respiratory center in the brain is depressed by toxic substances such as the narcotics and the barbiturates, when the diaphragm and intercostal muscles are paralyzed such as sometimes occurs in high spinal anesthesia, or when both these conditions occur, as in many cases of infantile paralysis, the maintenance of respiration by mechanical devices is vital.

At present the best method to maintain artificial respiration for any length of time is the use of the so-called iron lung or body-enclosing respirator. The National Foundation for Infantile Paralysis has been devoting large funds to experiments leading to the development of new devices without the disadvantages of iron lung equipment.

Investigators in the Physiology Laboratory of the Harvard School of Public Health, led by Dr. Stanley J. Sarnoff, conceived the idea of maintaining involuntary breathing by stimulating one of the phrenic nerves electrically. Animal experiments demonstrated that such respiration could be established and that a rhythmic beating could be maintained perfectly with submaximal stimulation of one phrenic nerve. Indeed the phrenic nerve was found to respond to electric stimulation not only when the electrode was applied directly to the nerve but also when stimulation was applied to the skin just over the point where the nerve transverses the lateral edge of the anterior scalene muscle. Stimulation applied to one phrenic nerve was found sufficient to establish respiration which would oxygenate the arterial blood.

A recent review of progress in this field by Doctors Stanley J. Sarnoff, James V. Maloney and James L. Whittenberger is published in the *Annals of Surgery,* November, 1950.

The method is undergoing continuous investigation and may prove of great benefit not only in the care of those with poliomyelitis but also in instances in which death would result under high spinal anesthesia without the possibility of proper application of artificial respiration until the effects of the anesthesia are overcome.

MORRIS FISHBEIN

Men of Medicine

A Pattern of Medicine, Flying and Guns

As a boy on a farm near Lock Haven, Pennsylvania, Malcolm Cummings Grow watched the hawks soaring above the serpentine Susquehanna and wondered about their effortless flight. He was only about nine, but he figured out that they were carried aloft by meeting air currents with flared wings; the currents, he was to learn later, were called convection currents. He envied the hawks. Like many another dreamer about aviation he thought he would have a try for himself. He got some turkey wings and nailed them to the side of the red barn to dry. Then, a barefoot Icarus, he tied them to his wrists and jumped 12 feet off the barn roof. The fall sprained his ankle, but did not knock out of him his dream of flight. This first injury was the only one that Malcolm Grow was to receive in more than 3,000 hours of engine-powered flight, including three forced landings.

Malcolm Grow got something else from his early years in the hills of central Pennsylvania—a feeling for guns. Even before he was able to hold up the muzzle-loading shotgun used for hunting in the 1890's he learned how to fire it, and to delight in the roar that echoed in the valleys. He learned still another thing from his years in the hills—how to conserve his strength in climbing. He learned the trick from the old-time hunter who taught him how to handle a gun. It was to take short steps while climbing hills, the short, efficient steps used by an expert mountain-climber to reach his goal.

Medicine was to come later, to be woven into the pattern of flight and guns formed in the farmlands of Pennsylvania. The three strands were to reach the final grand design only in World War II when the inquisitive, inventive boy had reached his 50's. If it had not been for his fascination with the soaring hawks and the roaring guns, and for the final thread of medicine added by seeming accident, many hundreds or perhaps thousands of American aviators would have returned to their homes badly wounded, or never returned at all.

Two peaks jut up in the career of mountain-climbing Malcolm Grow. One was the peak of adventure reached when he served in World War I with the Russian Imperial Army, and knew combat and killing finger-lengths away. The other was in World War II, when he saved lives by practical preventive medicine—an inclination that may have stemmed from the need for prevention of injury learned in the abortive flight from the barn roof. Aviation medicine means preventive medicine, not the most efficient way of killing the enemy from the air.

Today, his hair and eyebrows almost white but his blue eyes just as keen as they were when he hunted as a boy in Pennsylvania, Grow is recognized as one of the great pioneers in aviation medicine. The first Surgeon General of the U. S. Air Force, Major General Grow has now retired from that history-making job. It is a retirement in which he looks forward to the future as well as back to the past.

At the age of 11 Grow left rural Pennsylvania and returned to Philadelphia, where he had been born on November 19, 1887. His father had gone back to become state editor of the old *Philadelphia Record*. Young Grow went to public grammar schools, and then to Central High School. In high school, he was thinking of his beloved guns—not so much of planes—and he played with the idea of going to Annapolis or West Point. His father favored medicine for his son's career. Then the father became ill, and that fact tilted the scales to medicine; if he went to medical school, he could live at home. So he entered Jefferson Medical College when he was 17, after three years of high school, with enough credits for the less stringent qualifications of those days.

He was graduated in 1909 and began to practice in Philadelphia. For three years he taught internal medicine and physical diagnosis in the clinic at Jefferson. Then came a turning point in his life, and in the lives of future aviators who were then handling nothing more lethal than a rattle.

It was a hot and sultry August in 1915 that the young Dr. Grow talked to a Red Cross doctor in the Hotel Willard in Washington. The head of the Red Cross mission in Russia had just returned to this country and was looking for doctors to take back with him. The Red Cross doctor gave a picture of World War I medical conditions in Russia that was horrifying. One doctor tried to take care

MAJOR GENERAL MALCOLM C. GROW (RET.)

of a regiment of 2,600 men, compared with the U. S. average of nine or ten to a regiment; after a major battle, the doctor might, with the help of a few half-trained orderlies, have to handle as many as 2,000 wounded. Suddenly, the doctor said: "How about you going over with me, Grow?" General Grow tells the story in a book he wrote, in six weeks, in long hand, called *Surgeon Grow: An American in the Russian Fighting,* published in 1918. Grow now remembers the adventures told in the book with pleasure, the title with a shudder. He had left choice of the title to some friends and the publishers and had gone off to join the U. S. forces in Europe. By the time the friends and publishers, quite pleased with themselves, had told him the title they had picked (patterned after *Private Peat,* a popular World War I book) it was too late to do anything about it. Grow, not technically a surgeon, was so annoyed that he never kept a copy, and does not own one to this day. But his memory of the events described is clear.

The Red Cross doctor presented other arguments in favor of serving with the Russian Army. He pointed out that he would not only help men in pain, but would get experience in a few months that would be equal to years of private practice. Young Dr. Grow—he was then 28—was impressed, and added another thought of his own. He wrote in his book: "The doctor's eloquence had awakened in me an inherent love of adventure, a latent desire to see this great world tragedy, and a growing belief that the experience which I would gain in Russia would prove of some benefit to my country later on." It did. But the benefit that the Russian experience was to yield his country did not reach its height until another world war a quarter of a century later.

Two weeks after his abrupt decision Dr. Grow was on board the Russian munitions ship *Dvinsk.* A month later he was riding in a droshky to the brown-stone Astoria Hotel on Petrograd's St. Isaac's Square. There, he saw Grand Duke Michael. Neither Grow—nor the Grand Duke—had any idea of the scenes to be enacted at the hotel only two years later. Dr. Grow's first appointment, in October, 1915, was at the Hussars Hospital at Tsarskoe-Selo, "the village of the Czar," where, in peacetime, Czar Nicholas had a favorite palace. The wounded reached the hospital in terrible shape; many had spent four days on the train, lying on straw-covered floors of box cars, their bandages unchanged since they left the first aid stations.

Dr. Grow had a bit of luck—the kind of luck that happens to a wide-awake doctor. There was not enough antitetanus serum in Russia for adequate dosage in routine treatment of wounds. One soldier in the hospital had contracted a severe case of tetanus and was near death. But Grow managed to save his life with a massive dose of serum he got from a U. S. drug salesman who happened to be going about his business in Petrograd. Saving the man's life made a great impression on the Russians, and led to Grow's great adventure.

Soon he heard that Colonel Kalpaschnecoff was looking for a surgeon to replace one who had been killed by a German shell. The colonel was commander of the 21st Flying Column, attached to the First Siberian Army Corps; his corps had won, through its war record, the name of "Ironside Corps." The young American doctor found himself called officially "Malcolm Alvaovitch Grow." When he applied for a commission in the Russian Army officials asked him whether the "Cummings" was his father's name; he explained that it was his grandfather's. They took his father's name, Alva, and made it his middle name, Russian-style. He was commissioned a captain. But since he was a foreigner, his rank was raised one degree, and as far as uniform and honors went he became an acting *pot-pulkovneck* or lieutenant colonel; in the Russian army there was no rank corresponding to that of major.

Grow bought the required trimmings of a *pot-pulkovneck,* including a huge saber, high black boots, Persian lamb cap, and spurs. Then Grow was ready for the front, and a series of adventures that led to 13 major engagements and two wounds.

Grow found the Flying Column headquarters in an old Polish manor house. There he discovered that the Russians were efficient in at least one respect. He had arrived at night. By 5 A.M. the Russian general had found one of the few among his 50,000 men who could speak English. The English-speaking Russian soldier came to introduce himself to "your excellency" as his orderly, Michael. Grow asked him where he had learned to speak English, and Michael explained that he had worked six years in Pittsburgh steel mills. Many GI's in a later war were to tell similar stories of meeting Europeans who had learned English while in the U. S.

Grow soon found the prediction that he would get plenty of practice was true enough. During one battle he saw an average of 1,000 wounded a day for ten days. The only helpers he had were five medical students and some half-trained orderlies; often he had to do surgery in a shell-torn tent, tying arteries by candlelight. He wrote of the scene after one major attack: "In a night's work of that description a man performs more operations and treats more cases than the busiest practitioner sees in a month of private practice; and while conditions work havoc with technic, such an experience is a wonderful developer of resourcefulness. . . . It was a case of plodding through operations with dogged perseverance—a hurried amputa-

tion . . . an abdominal section—on and on without end." After one battle, less than 300 were left from a battalion of 1,200 men; the rest had been wounded, killed or captured.

One night he was so tired that he fell asleep in a barn, without looking closely at the eight or ten soldiers lying around the floor. Later, shells began to fall and he tried to arouse them, calling out "Galoopchick," Russian for "little dove," the usual greeting officers used for privates. They were very dead little doves; Grow had fallen asleep among the frozen corpses in a barn used as a mortuary. He ran out, and a few minutes afterward a shell demolished the barn.

Grow was not so lucky a little later. During a barrage, he started to run for a blindage, or bombproof, when a shell struck a tree nearby. The blast knocked Grow unconscious, and shell fragments pricked his skin, though not deeply enough to do much harm. The fragments had first gone through 20 inches of tough green wood, and so lost most of their velocity—a fact that may have stayed in his mind to reappear as a life-saving device for U.S. aviators 28 years later. He was deafened for a while, but soon was as good as ever.

Grow had another near-miss while with the Russians near Lake Maroch. He was eating dinner in the open when a Russian shrapnel shell case fell just four feet away, narrowly missing all of the diners. Grow kept the case for a while as a flower vase, but lost it later, along with other souvenirs, during the Russian Revolution.

The next time was closer. Grow had gone into a dugout, in a village just abandoned by the Germans, to look it over as a possible location for a dressing station. The dugout was dark. There was a flash as a German under-officer fired his revolver. Grow felt a stinging sensation in his abdomen and staggered out. He found that the bullet had just grazed him, and the only injury was a red crease across the skin. He had been "scutched," as old hunters of Pennsylvania would have said. Later, after the German was taken care of, Grow went calmly ahead and set up a dressing station in the dugout. Grow has always been a man to keep his eye on the job to be done.

General Grow and Russian boy, Poltava, Russia, September, 1944.

The Russian adventure gave him his first experience with aviation since his turkey-feather flight from the barn roof. It was against orders, but a friendly Russian aviator offered him a ride in a single-engined Albatross observation and bombing plane, which had been captured from the Germans. Grow sat in the observer's seat, and watching Germans scurrying for cover was reminded of "chickens at home when a hawk would float over them." Other Germans fired anti-aircraft shells at the plane which had none of the protection that Grow was later to develop. Luckily, the shells missed. On the way back, the engine went dead while the plane was still over German lines, but the pilot glided, like a hawk, to safety—with very little margin.

Grow's gravest danger in Russia was not from the Germans but from the Russians, during the October, 1917 Revolution. He had resigned his commission in the Russian Army Medical Corps, gone to America, and returned to Russia as a Red Cross doctor. Back in Petrograd, when the revolution was at its bloodiest, he and two British military observers—an artilleryman and an engineer—were in the Astoria Hotel, where Grow had stayed on his first trip to Russia two years before. The manager of the hotel was a Swiss who had known and liked Americans and Englishmen as tourists in Switzerland before the war. The Bolsheviks besieged the hotel, which had been taken over for Russian officers, their families and visiting foreigners, and snipers made it dangerous to get near the windows. The Russian officers fought off the revolutionists until they ran out of ammunition. Then a mob of civilians, soldiers, sailors and marines stormed the hotel. The manager spotted an intelligent-looking sergeant and talked soothingly to him. The American and British officers in rooms 523 and 525 were important men, he told the sergeant, and if they were injured, the U. S. and Britain would immediately declare war

on the new Russian revolutionary government. The Swiss hotelman used the revolutionists' current catchphrase; the sergeant must, he said, "protect the fruits of the revolution" by seeing that the foreigners were kept safe. The sergeant agreed, and posted a guard of marines from the Kronstadt outside their doors. It was lucky for Grow and the others that he did, for the revolutionists raided the hotel's wine cellars, and during the night slaughtered most of the Russian officers and their families. Though Grow and the British officers were safe, he could not tell about their narrow escape in his book. The book, published during World War I, was censored by the War Department. There was still some hope Russia might remain in the war, and the U. S. did not want to offend an ally.

The escape from the Astoria Hotel was not the end of Grow's Russian adventure; he still had to get out of the disorganized country. It took him two weeks to make his way across Siberia to Vladisvostok. When he got to Japan, it was just in time for a typhoon, and much of the country was flooded. He hired a sampan and for a day and a half sailed over what had once been dry land.

Back in the U.S., Grow was appointed a captain in the Medical Reserve on December 5, 1917. In April, 1918, he went on active duty at the Medical Officers' Training Camp at Fort Oglethorpe, Georgia, and in October sailed for France with the 45th Artillery, Coast Artillery Corps. His service with the U.S. forces in World War I was somewhat anticlimactic to the Russian adventure. He saw no fighting, but was busy at important, although routine, jobs. In December of 1918 he became surgeon of the First Machine Gun Battalion of the 42nd Infantry Division in the Army of Occupation of Germany. In March, 1919, he was appointed Sanitary Inspector of the Fourth Division of the American Expeditionary Forces. In Germany, he was able to get in some hunting, and shot some wild boars. In World War II he shot some of their cousins in France.

The dream of flying, born of the hawks and fed by the flight in the Albatross in Russia, never left Grow. In 1921 he applied for admission to the School of Aviation Medicine at Brooks Field, Texas. But, for obscure reasons, it was not until 1927 that he was admitted. He enrolled in January, 1928, and completed the course for aviation medical examiners. He was graduated in April of that year—beginning 21 years of association with the air forces. In the intervening years Grow had been too busy to fly and, until 1928, had not been in a plane since he left Russia.

Between the wars, Grow filled many posts in the Army; they were, again, routine, but helped prepare him for his great role in World War II. In July, 1920, he got his regular Army commission as a captain in the Medical Corps, and then was appointed supply officer of the Fourth Sanitary Train. He was also assistant surgeon of the Medical Department at Camp Lewis, Washington, and assistant surgeon of the station hospital at Fort Lawton, Washington. In June, 1924, he was appointed Post Surgeon at Fort Lawton and in September went back to Camp Lewis as assistant surgeon at the station hospital. In April, 1925, he was sent to the Chilkoot Barracks in Alaska where he again found time to combine military medicine with hunting and shot Alaskan bears and mountain goats and sheep. He also hunted moose in Canada successfully.

In 1933, Grow's double-barreled interest in aviation and medicine began to bring down big game. He saw the need for a medical aviation laboratory that would tackle the problem of keeping men fit and alive in the planes that were flying higher and higher. In 1935 he finally succeeded in getting the appropriation and set up the Aero-Medical Laboratory at Wright Field, Ohio, with the help of Harry G. Armstrong, now a major general and his successor as surgeon general of the Air Force. Grow made inquiries about what other countries were doing in this field and found that the U.S. was lagging behind. The U.S., for instance, had no oxygen masks. Pilots inhaled oxygen through a tube that worked efficiently only up to 18,000 feet; other countries were developing masks that were good up to 30,000 feet. Grow did not want to see his country outdistanced, as the Russians had lagged behind the Germans, in aviation. The new laboratory set to work to develop better gas masks, better types of winter clothing, and to decide such questions as how much carbon monoxide a flier could tolerate.

In the summer of 1934 Grow was flight surgeon with the famous Alaskan Flight. The history-making event was led by General Henry H. ("Hap") Arnold, then a lieutenant colonel. There were 12 B-10 bombers in the group, two-motored planes that could fly 165 miles an hour, the latest things in military aviation. They were old-fashioned by today's standards, with no variable-pitch propellers and no wing flaps, but they were far ahead of the Albatross and Farnum planes that Grow had seen in Russia. The airports were primitive, too. The fliers could land without too much trouble, but then the question of whether they could take off again often turned up. Little advance information was available, and the aviators would pace off the field to see what their chances were. All the planes got back to the U.S., one after a forced landing at Cook Inlet, Alaska. Because of the melting glaciers the water was not as salty as the ocean, and the metal parts were little corroded. The plane was towed to a dock near Anchorage,

General Grow, Lieutenant Colonel Jackson (at wheel) and "party"—Russian children, Poltava, September, 1944.

washed off in fresh water and flown back. The flight added little to Grow's medical knowledge; it helped Arnold on the way to fame.

After the Alaskan Flight Grow resumed his duties at Wright Field. In October of that year (1934) he became assistant chief of the Medical Division of the Air Corps, and in March, 1935, was appointed chief of the Medical Division, and served in that post until October, 1936. In February, 1936, he took part in another feat of aviation when he accompanied a ferry flight of 12 B-6 bombers and 13 P-12 pursuit planes from the U.S. to Panama. Grow acted as co-pilot on one of the bombers, although he was not ranked officially as a pilot. The flight made ten stops; now it would be made in one jump. The flight was not as important in aviation history as the Alaska Flight, but it did give Grow a chance to get in some tarpon fishing in Panama. From October, 1938, to May, 1940, he was flight surgeon at Langley Field, Virginia, and he then became surgeon at MacDill Field, Florida. In January, 1941, he was assigned as surgeon of the Third Air Force at Drew Field, Florida.

In all this time Grow had been gaining knowledge about aviation medicine. He thought it was time to put what he knew about it into writing for the benefit of young aviators then being trained for another world war just over the horizon. Grow, then a lieutenant colonel, and Armstrong, then a captain, got together to write *Fit to Fly: A Medical Handbook for Fliers,* published in 1941. As it turned out, Grow had to do most of the writing—again in long hand—as Armstrong was called away on other duties. Grow, a pioneer in modern aviation medicine, took a long look at its history. It was 120 years before the airplane was invented that the first studies were made in aviation medicine: a sheep, a duck and a chicken were sent up in a balloon, in France, in 1783.

There is a lot of down-to-earth medicine in this book written by two fliers for other fliers. The book's detailed medical section starts off sensibly enough with a discussion of the common cold, then goes on to more specific problems in aviation medicine. The book contains one of the two terms coined by the authors that have found a place in medical annals—aeroneurosis, a type of emotional stress that affects especially aviators' gastrointestinal tracts. They also first used the term aero otitis media, now more commonly called barotrauma otitis media, a condition caused by variations in air pressure and so common among aviators that it is almost an occupational disease. Amusingly, Grow praised mountain climbing and hunting in mountainous country as a good exercise for aviators.

In a prophetic paragraph, Grow saw the need in pre-Pearl Harbor days of preventive medicine for aviators and the need for detecting strain in a flier before he becomes "obviously fatigued" and so on the verge of breaking down. He wrote a prescription that he was able to put into effect with dramatic results in World War II:

> "In addition to providing adequate combat-crew personnel so that sufficient short rest periods are possible by rotation of duty while in active service, arrangements should be made for rest and recreation centers where personnel can go for longer periods of time. Conditions during these longer relief intervals should be such that the fliers are completely divorced from everything that pertains to flying. Facilities for exercise in the open air

such as golf, swimming, tennis, should be provided, plus such social activities as will tend to distract the mind from the recent stress of wartime military aviation."

Grow's ability to see that the prescription was filled came much sooner than he or anyone else imagined. In February, 1942, he was assigned to the office of the Chief of Air Corps at Washington. In June he was appointed surgeon of the Eighth Air Force at Bolling Field, D.C., and served as surgeon of that outfit in the European Theater of Operations, and later as surgeon of all U.S. Strategic Air Forces in Europe. He remembered the danger of aeroneuroses he had foreseen in peacetime, and knew that American aviators, far from their homes, needed a place to rest and recuperate. At first—this was 1942—he had a hard time convincing the British, whose fliers could go home easily enough for a week's rest. Then, when he brought up the idea of using great British estates for rest homes for U.S. aviators, he ran into another difficulty: the owners feared that the Americans would wreck their homes. Grow knew what he was doing. He told them that the better furnished the country houses were, the less the danger of vandalism; there might be trouble, he knew, if the houses were stripped down to a barracks-like atmosphere. Grow was right. There was no trouble with vandalism. Valuable collections of jade and tapestry were undisturbed; the war-weary fliers treated the country houses like homes for living, not like barracks for rough-house.

The first estate, "Stanbridge Earls," near Southampton, opened January 3, 1943, was the icebreaker, and Grow soon had enough homes to take care of 1,200 enlisted men and officers in any one week. The staffs as well as the furniture of the homes—finally, 40 of them—were left intact as far as possible, and the aviators were treated like weekend guests. They wore civilian clothes and could do pretty much as they liked, from breakfast in bed to visits to nearby pubs. They had all the sports they wanted—archery, boating, tennis—and could go on picnics or hikes. Red Cross girls acted as hostesses to increase the atmosphere of informality.

Flight surgeons were trained to notice early signs of a crack-up, such as brooding, withdrawal from companions, insomnia, unusual air sickness, combativeness, startle reactions, etc. It was important for the surgeons to diagnose the trouble before it really developed; if the men cracked up, it would take a lot more than a rest in the country to cure them. They were not likely to go to a doctor on their own; it would have been like admitting a weakness. Grow was practicing preventive medicine of a most effective kind. It is significant that during the first year of war not one case of psychiatric breakdown from combat was returned from the Eighth Air Force to the U.S.

It is hard to tell how many men Grow saved for combat. Since they were caught before breakdowns occurred, there was no medical history. It was prophylaxis, not cure. Grow made another important discovery. A week at the rest homes was the limit. After that, the men lost the desire to go back to the fighting; their team spirit was gone.

Development of the rest homes came largely from Grow's peacetime experience. But the development of body armor was a direct result of his observations in Russia; his thought that service in Russia might benefit his own country was thus made good in a dramatic way. While in Russia he had noticed that about 50 per cent of all wounds were from fragments of high explosive shells that lost their velocity rapidly. A check of early Eighth Air Force casualties, made at Grow's request, showed that about 65 per cent of all wounds were caused by missiles of relatively low velocity. So, he thought, why not try armor? Aviators did not have to climb out of trenches and go charging across No Man's Land, as soldiers had to in World War I. They could be protected by body armor, if something not too bulky could be developed.

Grow, like many other Americans faced with a tough problem in England, called on Scotland Yard for advice, and the Yard recommended the Wilkinson Sword Company in London, which had made bullet-proof vests for Chicago gangsters and also for some Eastern potentates. Grow had worked out a 12 per cent manganese steel formula for the thin plates of the armor, and Wilkinson's agreed that it was just about right. Grow then figured out the design of a suit of mail, weighing only 22 pounds, to cover the chest and abdomen. Wilkinson's made a sample suit, and Grow tested it by firing a .45 calibre Colt at point blank range. He knew that if the suit could stop such medium-velocity bullets, it would stop a lot of flak, which travels at low velocity. It stood up. Handmade suits were tried out on the crew of one B-17 in actual combat. The armor worked again. Then the crews of 12 B-17's were armored. These first tests were so successful that the body armor, often called a "flak suit," became standard equipment and was turned out by mass production in both Britain and the U.S.

At first, Grow had a hard time persuading the men to wear the suits. They were sure that, since the anti-aircraft shells were fired from the ground, the danger was beneath them. So they would set off on bombing raids over Germany sitting on stove lids. But they were skeptical about the need for protection from shell fragments or machine gun bullets coming at them from above and along side them—where, as a matter of fact, the real danger was. Later, Grow developed a helmet, often called a "flak helmet." Made of man-

General Carl Spaatz (left) shown with Brigadier General Malcolm C. Grow on the latter's appointment as Air Surgeon, Army Air Forces, to succeed Major General David N. W. Grant who is retiring.

U. S. Army Air Forces Photo

ganese steel plates and weighing two and a half pounds, it was stronger than the standard infantry helmet, although smaller.

The fliers soon learned to wear and respect their body armor and helmets as they saw casualties drop. They turned in dramatic reports of the way they worked. One bombardier, Lieutenant ——— ———, reported of his experience in October, 1943:

> ". . . I put on my flak suit just before hitting the French coast, and a short while later I was darn glad of it. . . . We hit the heaviest flak I've experienced to date and while looking out for fighters there suddenly came a ping and a shattering like ice in my face, a dull thud and an inch long piece of flak bounced off my flak suit onto the floor in front of me. . . . If I had not had the armor on I expect there would have been a messed up bombardier in our ship."

Another bombardier reported: "I . . . was struck by flak on the helmet. The fabric was torn and the steel plate dented. I was injured by flying pieces of plexiglass and stunned by the blow. I am indeed of the opinion that my flak helmet saved me from serious injury or death." The flight surgeon who examined him reported in more technical language: "Examination of the flak helmet of ——— ———, dented by flak . . . shows an indentation in the reinforced area of the right temporo-parietal region approximately 2½ inches in circumference and 1¼ inches deep. The projectile of flak, weight about 8 ounces, was found in the airplane. Without a suitable helmet of this type this officer would have undoubtedly been seriously injured if not killed."

Another of the hundreds of statements about nearly miraculous escapes said:

> "The formation was under attack by a number of Me 109's. They were attacking from above and behind. I was firing my gun in the radio room

when I was hit in the chest and knocked down. The blow knocked the wind out of me. I shouted over the interphone that I had been hit and began to put out the fire in my burning flak suit by hitting it with my hands. I then felt under the suit for blood, thinking I must be bleeding. I found no blood, so pulled myself up and started firing my gun at the attacking planes."

Still another report, telling of a slight wound from a .30 calibre bullet that might have been fatal except for the flak suit, said: "I'm getting the Purple Heart for my wound. If it weren't for the flak suit I'd be getting the Purple Heart posthumously. . . . So I'll say it again: 'Flak suit, I love you.'" So the stories ran, of men saved from death or mutilation; thanks to the genius of a man who knew guns and planes, and loved medicine.

Other preventive medicine gadgets were to come. Grow designed "casualty bags" in which wounded could be placed. They were electrically heated, to protect the wounded from cold that might, at 30,000 feet, be as low as 50 degrees below zero. They were also designed to serve as flotation suits, so that if a plane landed in the water the wounded man would float, and float face-up. Grow tackled the problem of frost-bitten hands, which were causing more casualties than German fighters or German anti-aircraft fire. The gloves then in use were too clumsy, and gunners would take them off in combat; in a matter of seconds their hands were frozen. Grow developed a thin, electrically heated glove that solved the problem. He also developed other electrically heated clothing, windscreens to protect gunners from windblast, combat rations, and so forth.

But Grow was forbidden by the Army top brass from making combat flights over Germany. He found that he could not circumvent regulations as easily as he did with the Russian Army in World War I, when he flew over German lines in the Albatross. One night he was in a bomber ready to take off for Germany when word got to headquarters, and he was ordered off the plane.

But he did manage to get in a good deal of flying. In 1944 he flew to the Ukraine, where the U.S. maintained bases for shuttle bombing, and Grow inspected three American hospitals. He also had a well-remembered trip to Africa in 1945 when, as chief guest at a dinner in Algiers, he was given the eyes from the whole roast sheep. He ate them.

One of Grow's most successful hunts was the round-up of German experts in aviation medicine during the closing days of World War II. First, Grow organized a team to pick up the scientists and collect all possible documents, equipment, etc., relating to their work. Then, some of the experts were persuaded to continue their work, under U.S. Air Force supervision, in the Kaiser Wilhelm Institute at Heidelberg. Much of it was in correlating and reviewing captured documents. Finally, under "Operation Paperclip," the German scientists were brought back to this country, and put to work at the Wright Field Aero-Medical Laboratory that Grow had helped to establish, and at the U.S. Air Force School of Aviation Medicine at Randolph Field, Texas. Among the 56 specialists brought over was Dr. Hubertus Strughold, who had been head of German research in aviation medicine. After nearly five years of research and translation, the most important papers were published last summer in a two-volume work called *German Aviation Medicine in World War II,* issued by the U.S. Government Printing Office. Most of the job was done while Grow was Surgeon General of the Air Force, although it was published after his retirement.

The work reveals that in some ways German scientists were ahead of the U.S. But one thing they had not tried was body armor. After they got some samples of Grow's flak suits from captured fliers in 1943, they admired the suit, but could not duplicate it because of shortage of materials. As the war ended they were experimenting with synthetic materials, but they never got around to making anything as good as Grow had made for the U.S. Air Force.

Grow's developments in preventive medicine helped in the war against Japan, but he arrived too late to see much of actual combat. In August of 1945 he was appointed surgeon of the U.S. Strategic and Tactical Air Forces on Guam, and so arrived when the war was about over. He flew over Nagasaki and Hiroshima and saw what the atomic bomb had done, and inspected from the air 20 other bombed Japanese cities. While flying over Tokyo Bay he came pretty close to repeating, more disastrously, the barn-roof casualty. One of the engines on the four-engined plane caught fire, but the bomber made a forced landing safely.

After the war with Japan was over, Grow came back to the U.S. and was named Acting Air Surgeon. In January, 1946, he was named Air Surgeon. On July 1, 1949, he was appointed Surgeon General of the U.S. Air Force Medical Service—which had just become independent of the Army—and thus became the first Surgeon General of the Air Force. The appointment meant that aviation medicine had come of age, and that the Air Force medical department had won equal status with that of the Army and Navy. It was something that Grow had believed in passionately and worked for assiduously in the postwar years. To a great extent it was due to Grow's character that the history-making decision was made. Grow had ability, and belief in his own ability, but above all a belief in the importance of aviation medicine. He had gained, through the years from the Pennsylania hills to the Siberian Army Corps, a medico-

military technic. It meant the saving of lives, and it meant, finally, that aviation medicine was at last air-borne.

For all his work in the field of military medicine and aviation, Grow has won many awards. Among the first was the Medal of St. George, Third Grade, given to "Malcolm Alvaovitch Grow" by the Grand Duke Nicholas while he was serving with the Russian Imperial Army. The Grand Duke told him: "Malcolm Alvaovitch Grow, you have been mentioned by the commander of the first division in dispatches to our Emperor. These dispatches told how you stuck to your post through most trying circumstances, caring for our wounded Russians, although warned by Colonel Starik to retire, and how you set for your orderlies and our soldiers an example of devotion to duty and bravery. For this the Emperor desires that I thank you and present to you the Medal of St. George." Grow also received from the Russians the Cross of St. Stanislaus with Crossed Sabers and the Medal of St. George, Fourth Grade.

His most recent award was given him by the Association of Military Surgeons of the United States in November, 1950. It was the Gorgas Award of 1950, consisting of a silver medal, a scroll and $500 in cash. The citation read: "For distinguished service to our military forces in furthering the conservation of fighting strength of air fighting crews. He initiated, developed and made final arrangements for the employment of body armor to protect these fighters. He developed and put into use a device to protect gunners from wind blast; he developed electrically heated clothing, casualty bags for the wounded, and wind and fire resistant face and neck protectors. He thereby not only saved life and suffering to flight crews but added immeasurably to their combat efficiency."

From the U.S. he received the Legion of Merit in July, 1943; the Distinguished Service Medal in 1944; the Bronze Star Medal in December, 1944. He is authorized to wear the Army of Occupation of Germany Medal (January, 1918 to August, 1919), World War I Victory Medal, World War II Victory Medal, American Defense Service Medal with Foreign Service Clasp and Bronze Service Star, and the European and Pacific Theater ribbons. In 1949 an oak leaf cluster was added to the Distinguished Service Medal. Foreign countries in addition to Russia have honored him: in 1945 he was awarded the French Legion of Honor with the rank of Chevalier and the Croix de Guerre with Palm; in 1947 Belgium gave him the Croix de Guerre 1940 with Palme and in 1946 Italy gave him the Cross of the Grand Officer in the Order of the Crown of Italy. Britain made him, in 1947, a Commander of the British Empire. He is a member of the American Medical Association, fellow of the Royal Society of Medicine (British), a Temporary Associate Member L'Academie de Chirurgie de France, and an honorary fellow of the American College of Surgeons. In 1949 he was certified by the American Board of Preventive Medicine and Public Health. The Institute of Aeronautical Sciences gave him the John Jeffries Award in 1947.

Grow has written widely on the subject of aviation medicine. One of the more important of his papers was "A Study of Fatigue," in *The Military Surgeon* in February, 1946, in which he stressed the importance of the central nervous system in studying fatigue—from which General Grow himself rarely suffers. Other publications include: "Research in Aviation Medicine," in *The Army Medical Bulletin,* 1935; "Preliminary Report on the Effect of Cold on the Oxygen Content of the Blood," *The Military Surgeon,* 1949; an article on exhaust gases in the French magazine *Revue de l'Armee de l'Air,* 1935; "Aviation Medicine in World War II," in *Treatment;* "Age and the Fighter Pilot," with General Armstrong, in *Flying,* 1942; "Current Problems in Aviation Medicine," in *The Military Surgeon,* 1948; "Aero Medical Programe in the Army Air Forces" and "Medical Problems of the Military Establishment," both in the A.M.A. *Journal* in 1948.

In the time since his retirement on November 30, 1949, General Grow has been "resting up." For Grow, that has meant a toughening up process; he had been tied down to desk work for too many years. So he has been busy with gardening and landscaping for his one-story ranch-type home at Annapolis, Maryland, where he lives with his wife, the former Winifred Rogers, whom he married in 1930. Several times a week he drives the 40 miles to Washington, taking about an hour and a half—a very un-Air Force speed, but one that is reasonable for traffic conditions around Washington. Soft-voiced and dignified (his only nickname is a rarely-used "Mac"), he keeps a desk in the offices of the Surgeon General of the Air Force, and acts as consultant to the post he did so much to create. When not at his desk, or working at his home, he finds time for a little hunting or fishing (fresh water, light-tackle fishing preferred).

At 63 and nominally retired, General Grow is not quite sure what he will tackle next. His hands are callused from his gardening, and he feels in good shape again. He is now getting the range on the future. When he decides just what he wants to do he will set out for his goal with the short, efficient steps of the climber who knows where he wants to go, and the best way to get there.

GEORGE R. BURNS

Consultation Service

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USE OF PANPARNIT IN RHEUMATIC DISEASES

QUESTION: I read a report from a Swiss medical journal on the use of PANPARNIT in rheumatic diseases of the joints with good results in a small series of cases. Has there been any work in this country on the use of this drug and with what results?

M.D.—Georgia

ANSWER: "PANPARNIT" is the registered trademark of a synthetic compound (diethylamino-ethyl-1-phenylcyclopentane-1-carboxylate hydrochloride) with antispasmodic properties but without the antisecretory effect of atropine and related drugs. This chemical, apparently first developed and tested in Switzerland, resulted from a search for more effective therapy for various extrapyramidal diseases, particularly Parkinson's syndrome. It is stated that "the main effect of panparnit is the reduction of rigidity. . . ."[1]

Patients having parkinsonism may have associated periarticular limitation of certain joints, especially of the shoulders and fingers and sometimes also of the knees and elbows. When this occurs periarthritis is secondary to the primary disease rather than evidence of primary intra-articular disease or arthritis. When treatment for the primary (neurologic) disease results in satisfactory control of the symptoms and signs of the disease, improvement of articular function also may follow.

A clinical trial of panparnit in rheumatic disease was made at a Budapest hospital and reported in a German medical journal (published in Switzerland).[2] The report concerns the results of treatment of only 4 patients: 2 patients 19 and 43 years of age with "febrile polyarthritis" of three and four weeks' duration, respectively; 1 patient, 17 years of age, with "low grade joint disease" of six months' duration, and 1 patient, 55 years of age, with "articular rheumatism" of four months' duration. Evaluation of both the patients' condition and the results of treatment is made difficult by the brevity of the report. The author admittedly proposed the trial of panparnit for rheumatic diseases on a theoretical rather than a factual basis.

Perhaps it is significant that other antispasmodics, such as atropine, belladonna, and hyoscine, have not been found to have specific value—or to be of even consistent benefit symptomatically—in the treatment for rheumatic disease. The answerer is not familiar with any further published or unpublished studies regarding the results obtained from use of this chemical for articular diseases.

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1. SCHWAB, R. S., and LEIGH, DENIS: Panparnit® in the treatment of Parkinson's disease. J.A.M.A. 139:629-634 (March 5) 1949.
2. POLICZER, M.: Die Verwendung von Parpanit bei rheumatischen Gelenkserkrankungen. Schweiz. med. Wchnschr. 78:962-963 (October 2) 1948.

TREATMENT OF PSORIASIS OF THE NAILS

QUESTION: What can be offered for treatment of psoriasis of the nails of three years' duration in a 27-year-old white male? No evidence of the disease elsewhere on the body. The patient also has a severe seborrheic dermatitis of the scalp which responds with some favor to treatment.

M.D.—Nevada

ANSWER: The treatment of psoriasis of the nails of three years' duration offers a very resistant situation. As there is no evidence of the disease elsewhere on the body, it is very desirable to make several repeated examinations, both microscopically and by culture, to make sure there are no fungi present. There is no question that psoriasis does occur confined to the nails alone.

In regard to the severe seborrheic dermatitis of the scalp, it would be well to take a section to make sure this is not psoriasis, because 3 cases of seborrheic dermatitis of the scalp with nail dyscrasia seen in the past few months have responded very well to treatment.

Histologic examination of a portion of the involved nail plate would be very well worth while to confirm a diagnosis of psoriasis.

As far as treatment of psoriasis of the nails is concerned, it is like psoriasis elsewhere. It is extremely resistant to treatment, but many things have been offered for its amelioration. If it is really psoriasis a cure cannot be obtained at the present time with our present knowledge.

An ointment to use locally would be a 10 per cent salicylic acid and 20 per cent ammoniated mercury in a petrolatum base. This should be applied to the nails twice a week. All of the loose debris should be removed either by a scalpel or by the use of a small dental burr. Internal treatment, of course, theoretically should be of help—the use of vitamins A and D in large doses has been of some assistance in some of these cases. Fractional x-ray therapy may be used, 80 r once a week for

six times. Care should be exercised in keeping far short of an erythema dose on the glabrous skin, because the nails as a rule do not tolerate x-ray therapy to any marked extent. In cases of generalized psoriasis of the glabrous skin and nails, the use of ACTH and cortisone has succeeded in bringing about a temporary arrest in some cases. All in all, no matter what is used at the present time, there is a tendency to relapse on the nails as well as on the skin.

CLEVELAND J. WHITE

URINARY INFECTION FOLLOWING CEREBRAL HEMORRHAGE

QUESTION: Will you please advise me as to the treatment of an infection of the urinary tract in a patient in her middle 70's. The infection occurred following a cerebral hemorrhage and thrombosis on June 1, 1950. At times there is severe pain over the region of the bladder. There is often burning on urination; at times there is a purulent discharge, cheesy in appearance, coming from the urethra. At times a catheterized specimen shows 8 to 10 pus cells per microscopic field and sometimes there are 25 to 30 cells per field. On one occasion the urine was almost pus-free. Recently we tried Thalexal (Sharp & Dohme). The patient's nurse tried to wash out her bladder with saturated solution of boric acid; the patient resisted saying it was very painful. We have used a combination of codeine ¼ gr. and aspirin 10 gr. for the pain.

What would you suggest in the way of treatment to clear up this condition in the bladder? Any suggestions you may wish to make will be greatly appreciated.

M.D.—Michigan

ANSWER: Certain data in the history of this patient which might be helpful in arriving at a diagnosis are those pertaining to urinary symptoms before the thrombosis or the cerebral hemorrhage. Did the patient have any attacks of pain comparable to what she now has? What other urinary symptoms did she have previously?

It seems to me from the history and the course of events that this patient has some interference with drainage from her bladder coincidental with the vascular accident, and she now has a certain amount of residual urine, with quite a little difficulty in urinating. I dare say that this patient is passing an overflow at the present time, and pyuria is found sometimes and not at others.

A catheterized specimen of urine should be taken and a culture made of this urine. The patient's urinary infection should be treated in accordance with the types of organisms that are found, using the proper chemotherapeutic agents or antibiotic. Drainage of the urinary bladder with a permanent self-retaining catheter for a week or ten days should allay the symptoms this patient has.

Another condition one must think about is obstruction or narrowing of the urethra, which condition is often overlooked in older women, and is exaggerated by infection or pyuria.

I would continue to use the codeine ¼ gr. and aspirin 10 gr. when necessary to control the pain, although I believe that as soon as one drains the bladder thoroughly the pain will disappear. Start the treatment for the infection two or three days prior to the catheterization, so that the introduction of the catheter will not activate another attack of pyelonephritis, with elevation of temperature and chills.

GILBERT J. THOMAS

TREATMENT OF SEXUAL INFANTILISM

QUESTION: I have a 15-year-old female patient who has the size, habitus and mannerisms of an 8-year-old child. Not only dwarfed, she has never had a menstrual period. She has, however, a very high I.Q. and consistently makes the highest grades in school.

There is no breast development whatever; her body, like her face, is round and plump and child-like.

I would appreciate any information you could give me on latest endocrine approaches to this problem. I have also read somewhere of an antibiotic with a hormone-like effect suitable to this case of infantilism.

M.D.—New York

ANSWER: The case referred to is one of sexual infantilism. The etiologic factors may be several. Among these must be considered (1) primary hypo-ovarianism, (2) hypopituitarism, (3) marked delay in pubescence. Of value in ascertaining a diagnosis would be the determination of urinary gonadotropins. If the titer is markedly elevated, it would point to primary hypo-ovarianism, which to me, in this particular case, is the most likely diagnosis. The bone age, the basal metabolic rate and the vaginal smear would be of considerable help. It would be important to rule out metabolic and systemic diseases as a factor responsible for the retarded development. If these questions are answered and point to a diagnosis of primary hypo-ovarianism, this is the treatment recommended:

Substitutional therapy by prolonged administration of estrogens, i.e., 0.02 mg. of ethinyl estradiol or its equivalent, twice daily for 20 days in each month. As adjunctive therapy for the sixteenth through the twentieth days of this regimen, the patient should also take anhydrohydroxyprogesterone, 10 mg. three times a day. If this regimen is carried on for an indefinite period, withdrawal bleeding may be expected with a certain degree of regularity after the second or third month of therapy and for as long as therapy is continued. Breast development, genital maturation and growth of sexual hair may also be expected.

The antibiotic with hormone-like activity referred to is probably aureomycin, but its use, as well as that of vitamin B_{12} in promoting growth, is experimental and its effectiveness has not been substantiated.

ROBERT B. GREENBLATT

DR. Pepys' Pages

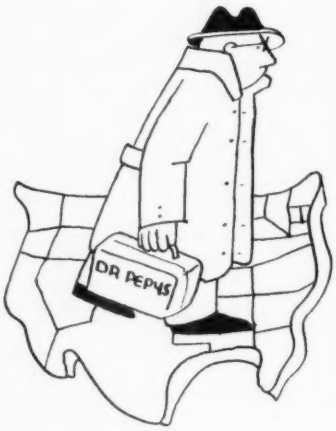
Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Nov. 27—Monday, with stacks of mail from far places and many deadlines to be met. In the evening to lecture to the young men and women at the University of Chicago on medical writing, and discovered that the preliminary requirements for medical education still insufficient to give students a basic understanding of grammar or composition.

Nov. 28—For luncheon at the Tavern Club with Leo Burnett. In the afternoon on a T.W.A. Constellation to New York, reading en route "The Infinite Woman" by Edison Marshall, which is a warm novel about a passionate dame—based largely on the life of Lola Montez. As she passes from bed to bed one wonders why she never conferred on posterity her technic for contraception—and the same applies to "Forever Amber."

Nov. 29—To breakfast with Bill Frohlich of New York and Peter Warren from Amsterdam. Then meeting with Buchthal and Ragoczy, Basil O'Connor and all the staff of the Polio Foundation arranging for the International Congress on Poliomyelitis to be held in Copenhagen in September, 1951. In the afternoon driving with Greenwald and Van Riper to New Haven. Here the beautiful new home of the Connecticut State Medical Society demonstrated by Grace Mooney, including a beauteous room called a powder room for the ladies and one also for the men and upstairs a location for the Middlesex Medical Society. Also a great room wellnigh filled with about a ton of Whitaker-Baxter ammunition, not yet distributed although the election some weeks gone.

To the Country Club where came all the officers and delegates of the state medical society to pay honor to Tom Murdock, newly elected a trustee of the A.M.A. Here speeches by Creighton Barker, secretary of the society, Wilcox of the International Silver Co., Stanley Kenney, president New York State, Alex Burgess, for the American College of Physicians, and by Van Riper and Eddie Cunniffe, who waxed eloquent on the seven stages of a man's life.



Old Pepys spoke of friendship and its meaning! And the best remarks on this subject were made by that great author "Anonymous," who said: "It is better to have one friend of great value than many friends who are good for nothing." Or perhaps: "Choose thy friends like thy books, few but choice." So Tom thanked every one graciously and received a scroll and a folder of testimonials and a big silver bowl and we drove back to New York, accompanied by Kenney, telling merry tales till we came into the Bronx.

Nov. 30—At breakfast in the Norse Grill—and saw Phil Hench and his lady and the family off to receive the Nobel prize for discoveries in rheumatoid arthritis. After some talk with Francis Brown of Schering to luncheon with Ralph Beebe, Mel Evans and Tom Burns of Doubleday and with them to confer with Donald Armstrong and his associates at the Metropolitan Life. In the late afternoon to visit Jules Stein in his beautiful room atop the offices of the Music Corporation of which he is president although previously a good ophthalmologist and assistant to Harry Gradle.

By the plane back to Chicago reading the life of "Sir Thomas Browne," by J. S. Finch. Of Browne, Sir William Osler said: "Mastery of self, conscious devotion to duty, deep human interest in human beings—these best of all lessons . . . may be gleaned from the life and from the writings of Sir Thomas Browne." And found the book full of quotes from the diaries and letters of Browne and his family giving it all the charm of Samuel Pepys' diary.

Dec. 4—A long week end with time for reading and writing and television. This night to lecture at the University of Chicago on "Fads and Quackery in Healing." With Hadacol the technics of patent medicine salesmanship approach the magnitude of the grotesque.

Dec. 5—To view the exhibits of the American Academy of Dermatology, greeting again many exhibitors and the dermatologic leadership. In the evening to a reception designed by Charles Revson and Mark Soroko of Revlon. Here were O'Leary and Forster and Rattner and Chuck Rein, and many others from far and near for a happy evening.

Dec. 6—By the late afternoon train to Denver, en route amused with Josephus Daniels' "The Man of Independence" which helps a little but not enough to explain H.S.T.

Dec. 7—Early to the University of Colorado Medical School and walked about with Ward Darley seeing the tremendous development that is making this truly a medical center, with all the problems of adjustment to the changing nature of medical practice. At noon to luncheon with Philip Houtz and the board of the Na-

(Continued on page A-50)